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INTRODUCTION

By G. W. T. H. FLEMING, M.R.C.S., L.R.C.P., D.P.M.,

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THE first edition of *Recent Progress in Psychiatry* was conceived and produced under war conditions which severely handicapped everyone and, owing to the paper shortage prevailing at the time, led to a much smaller printing than would otherwise have been. The present edition has provided problems of a different nature, partly owing to the flood of psychiatric literature (which shows no signs of abating) since the end of World War II. Some chapters have been omitted and will be dealt with in the third edition due in 1955—those on child psychiatry, psychopathic personality, manic-depressive insanity, convulsion therapy, and anatomy.

Too short a time has elapsed since the "appointed day," and the situation is too fluid to present a really sound description of the mental health services.

The danger of too much lay control of medical work is very real, and psychiatrists would be well advised to keep all the control they can over medical matters and not allow laymen to dictate policy, treatment or anything else to them. The position is in danger of getting out of hand, and it has been obvious for some years that unless a firm stand was taken this would happen. The medical profession have only themselves to blame for allowing it, a firm stand has *not* been taken, and instead of dealing firmly with administration, it has been allowed to pass into the hands of those who have not got the best interests of the patient in view.

A number of new journals have appeared in America and on the continent. One of the most useful being *Excerpta Medica*, published in Amsterdam. Section VIII deals with Neurology and Psychiatry, and is quite indispensable in every mental Hospital.

There have been no outstanding discoveries in the period covered by this review, but both prefrontal leucotomy and electric shock treatment have developed, particularly the former. The Anglo-American Symposium, arranged by Dr. Sargant at the Royal Society of Medicine in September, 1949, was an outstanding event in psychiatric history, and the appearance of the large tome by the Columbia-Greystone Associates, edited by Mettler and entitled *Selective Partial Ablation of the Frontal cortex*, was another.

It is with deep regret that the deaths of three contributors to this volume have to be reported. J. Tylor Fox, M. B. Brody and D. S. Fairweather did not live to see their contributions published.

The work done by the various contributors is much appreciated and the thanks of all psychiatrists go out to them.

PSYCHIATRIC GENETICS.

By ELIOT SLATER, M.D., F.R.C.P., D.P.M.,

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With a Section on

CAPILLARY MICROSCOPY IN PSYCHIATRY.

By J. W. LOVETT DOUST, B.Sc., M.B., M.R.C.P.

GENETICS AND PSYCHIATRY.

PSYCHIATRIC genetics do not, at first sight, seem to have much immediate and direct consequence for practical clinical psychiatry; and one might have imagined that years which saw almost the entire world submerged in war would have brought but little progress in this field. This has not been the case; indeed, the lessons taught by war have added to our understanding of environmental and constitutional interactions. There has, however, been an increasing tendency among clinicians to minimize the effects attributable to genetical causes, and to teach a psychiatry in which they receive little or no mention. This tendency has been marked in Britain, but it has assumed formidable strength in the U.S.A. Instead of a harmonious development, in which the psychoses and neuroses, constitution and environment, psychogenesis and physiogenesis receive their due share of attention, interest among practical workers has been devoted more and more exclusively towards psychotherapy, psychoanalysis, social psychiatry, personnel selection, group therapy, and preoccupations with anthropology, sociology and political theory. In its one-sidedness, this development is not healthy.

It is a sign of bad omen that it is possible for text-books of clinical psychiatry to appear, with claims for comprehensiveness, in which no mention is made of the established facts of genetics and of the hereditary element in mental disorder. Their authors appear to feel, though in fact this view depends on a misapprehension, that recognition of a hereditary factor implies a therapeutic nihilism; and that an energetic and optimistic attitude towards treatment calls for a neglect of hereditary factors, just as a due appreciation of the patient as an individual demands forgetfulness of nosological entities. One suspects that the prime motivation is derived from the philosophy of Dewey, which is no doubt over-simplified in the notion that one should accept as true that which has convenient practical applications.

It would not perhaps be putting it too high to say that we are witnessing the manifestation of an anti-scientific tendency which is winning an increasing number of supporters. The customary canons of scientific reasoning are ignored by these schools. Uncomfortable facts are left unconsidered. Hypotheses are multiplied regardless of the principle of economy. Explanations which may be valid for certain members of a class of phenomena are regarded as true for the class as a whole. Interpretations which conform with theory, and which might be true, are regarded as established. Possible alternatives

are not considered, and no attempt is made to seek for evidence of critical value which shall decide between them. Criticisms from outside are ignored, and only the initiate may be heard. Utterance is dogmatic and arrogant and lacks scientific humility and caution. These are the mental mechanisms which we associate with the growth of a religious orthodoxy, and not with the progress of science. The movement is of significance to genetics, because it is likely adversely to affect the personnel and facilities for research, and to lead to a psychiatry without biological foundation and divorced from contact with the other natural sciences.

The extreme emphasis placed on the environmental causes of mental disorder, most noticeable in American schools of psychiatry, is in close harmony with the American attitude to life, with a boundless optimism and a belief in the equality of man. This comes to be expressed in the concept of a limitless plasticity of human nature. In this view the psychiatrist has not lacked the support of one high genetical authority. Dobzhansky and Montagu (1947) argue that in one sense man is unique and not comparable with other animals. His self-made environment is immensely variable, and for him a genetically controlled plasticity is of selective advantage and not a genetically controlled fixity of traits. Man has freed himself from the need to adapt genetically, and does adapt through learned responses and new inventions. The survival value of this plasticity has probably been considerable for a long time on the human historical scale. Kallmann (1948c) has replied to this by pointing out that, however plastic and adaptable human personality is, mental behaviour remains a function of the organic nervous system. The biological process of personality integration at no time ceases to be subject to the laws of structural growth. Organic inheritance must therefore remain important. Unless hereditary factors are posited we are unable to explain why, under the same environmental circumstances, some individuals break down and others do not. He illustrates this by a discussion of his own schizophrenic twin material. Other criticisms of the argument of Dobzhansky and Montagu might have been made. The changes which are made by successive generations are toward reducing the impact of the environment; it becomes, in fact, progressively easier for the unadaptable man to survive and reproduce. When they say that natural selection favours the higher development of mental capacities in man, they are making a gratuitous assumption. The concept of genetically controlled plasticity or fixity of traits is, however, a valuable one; and the way in which it might work out on the evolutionary time-scale might be a matter for further investigation.

A novel and stimulating discussion of the interaction of nature and nurture has been provided by Haldane (1946). Let us suppose that two genetically different populations, A and B, are subjected to two environments, X and Y, and that they are subsequently examined in respect of a character which can be either measured or graded. Then the four interactions, AX, AY, BX, BY, can be ranked in order. With AX as 1, there are only 6 such orders, and these themselves can be classified into four types. In the first type (with AX, AY, BX, BY ranking respectively as 1234 or 1324) both one population and one environment consistently excel the other. In the fourth type (1342 and 1432)

the two populations react in opposite directions to the two environments. In the second type (1242) one environment is consistently better for both populations, but the two populations show no consistent difference between themselves; in the third type (1243) the converse is true. Haldane gives biological examples of observations of every type. In the perfect eugenic society the first and third types would be missing, and in the perfect environment the first and second. The ideal society would be of the fourth type, where every existing environment would be the best for one of the existing genotypes, and every genotype would be able to find its best environment. Above all, our aim should be to eliminate interactions of the first type. This discussion, though it sounds like a *jeu d'esprit*, is clearly of high practical applicability. Haldane points out the undesirability of restricting variability either of genotype or environment. "We are not justified in condemning a genotype absolutely unless we are sure that some other genotype exists which would excel it by all possible criteria in all possible environments." The eugenicist must pay due attention to this argument, although he will be inclined to give its maximum meaning to Haldane's "absolutely."

There is, unfortunately, inadequate space in this review for any general and documented discussion of the literature which has appeared on general and human genetics, but mention must be made of some items. Gates's *Human Genetics* (1946) is an encyclopaedic survey of the entire field. Despite some weaknesses, and the expression on some subjects of views which have failed to find support elsewhere, this will remain an invaluable work of reference. Another useful work of reference is Dahlberg's monograph (1943), a mathematical discussion of the changes in populations which may be caused by mutation, selection, inbreeding and assortative mating. The various modes of inheritance, dominant, recessive, sex-linked and autosomal, are separately considered; but multifactorial inheritance has not been given the amount of attention it deserves. Finally, a little book by Grueneberg, on animal genetics (1947), is of great interest to the student of human genetics. Grueneberg points out that there are many advantages in genetical work on animals. The disease studied is pure, as it can be specifically bred for. However "rare," the experimenter can breed as many examples as he wishes. The environment can be completely controlled. Above all, the experimenter can go back to as early a stage as he wishes in his quest for the pathogenesis, even if this takes him into early foetal life. The lessons that can be learned from such studies are important. It is repeatedly shown how phenotypically very varied states may be traced back to a unitary morbid process, and that their differences may depend on such minor deviations as a very slight delay in the time of onset of the first changes in embryonic life. The chapters on the diseases of the nervous system in the rat and mouse are of special interest to the psychiatric geneticist.

The literature on the most general aspects of psychiatric genetics has not been of great importance. Annual reviews of the literature have been given by Kallmann (1944, 1945, 1946a, 1947, 1948a) which cover, in very brief span, the work which has appeared from 1939 to 1947, and provide a bibliography. Penrose (1944), in a chapter of Hunt's book on the Behaviour Disorders, covers

in compressed form most of the topics of significance to psychiatry: methods of investigation, assortative mating, twins, linkage, intelligence, special skills, handedness, sense deprivations, aphasia, racial differences, normal personality and its pathology. Kretschmer has edited in a small volume a review of the whole of the psychiatric work in Germany during the war years. The German work on heredity in the psychoses will be considered under individual authors later; but the other of the two themes in this book which interest us may be taken here.

CONSTITUTION.

G. Mall, in the review edited by Kretschmer (1948), contributes two chapters on constitutional physiology and constitutional psychology. The latter, covering such subjects as muscular tonicity, school achievement, intelligence, musical ability, etc., contains little that is new or of much interest. The chapter on the somatic aspects of constitution, with over 100 references, describes lines of work that have not been touched outside Germany. The frequencies of the various constitutional types in a number of physical diseases have been investigated. In diabetes mellitus and in hyperpiesis, for instance, approximately 75 per cent. of the patients are pyknic; whereas in phthisis and in peptic ulceration, nearly two-thirds are leptosomatic. The varying dietetic habits of the three somatic types have also been investigated, and the relation of body build to haematology, albumin metabolism, etc. The work suffers from the disadvantage of a primitive statistical methodology. It would have been a considerable improvement if the whole concept of types had been abandoned and replaced by the use of bodily measurements or indices with means and standard deviations, and of regression equations where the covariance of two measurable variables was considered.

The most consistent and intensive effort to add to our knowledge of bodily build and its psychological relations has been made by Sheldon and his co-workers (Sheldon, Stevens and Tucker, 1940; Sheldon and Stevens, 1942), conveniently summarized by Sheldon (1944). These workers photographed a very large number of normal subjects, and all bodily measurements were made on the photographs. This is clearly a great technical advance in speed and efficiency of measurement, though it has drawbacks. Three dimensions of variation were used: endomorphy, i.e. relative visceral development; mesomorphy, relative bony and muscular development; and ectomorphy, relative fragility and delicacy of bony structure. The photographs were classified on a 7-point scale in each of these dimensions. Other physical traits, such as bisexuality, aesthetic harmony of structure, pigmentation, hair, secondary sex characters, were noted, but so far have not been specially studied. By means of associated psychological investigations the three physical dimensions were correlated with three temperamental dimensions, those of viscerotonia, somatotonia and cerebrotonia. Viscerotonia shows itself in relaxation, love of comfort, sociability; somatotonia in vigour and assertiveness; cerebrotonia in restraint and inhibition. The correlation between corresponding physical and mental variations are of the order of $+0.8$. These findings, the authors say, "contradict the current academic supposition that physical

constitution plays only a small part in motivation and temperament." Sheldon points out that a great advance is involved in the use of a dimensional frame of reference over that given by the concept of types, and that both physique and temperament must be regarded as subject to continuous variation.

Interesting and valuable as this work is, it has some fundamental weaknesses. Variation in stature, which without any doubt has very important relations to variation in temperament, has been entirely neglected. The measurements on the photographs were taken as ratios to height, which therefore disappears from the picture. Then the curious practice was followed of setting dimensions of variation which should be not independent of one another, but positively or negatively correlated. Sheldon's three dimensions, both of physique and temperament, have negative correlations with one another. This means that they are to some extent measuring the same thing. The statistical technique involves elements both of arbitrariness and confusion, and cannot be called satisfactory. The effort should surely have been to seek for dimensions of variation which were, as far as possible, independent of one another.

In this particular respect the work of Rees and Eysenck (1945) is to be preferred. These workers investigated 100 normal soldiers and 200 successive admissions to a neurosis centre, and analysed their results by factor analysis. They separated two main variables: one of size, which accounted for 34 per cent. of the total variance of the 18 measurements made; and one of body type, i.e. of development predominantly in length or breadth, which accounted for 12 per cent. of the variance. Neurotics proved to be more variable than normals; and towards the leptomorphic extreme, patients suffering from anxiety, depression and obsessions tended to be concentrated towards the eury-morphic extreme cases of hysteria. Rees (1944) has also reported investigations on 42 manic-depressives and 49 schizophrenics. Both groups were significantly smaller in stature than the normal group, but the manic-depressives tended to be eury-morphic and the schizophrenics leptomorphic—thus confirming one of the main results of Kretschmer's pioneering work.

An entirely new theme in the investigation of the constitution has been opened by the work of Bleuler and his associates. This will be discussed in detail later, but one aspect of the work may be mentioned here. Bleuler and his school have made a persistent effort to analyse the effect of various endocrinopathies on temperament, on the clinical features of psychopathy, and on the course and clinical picture in the psychoses. Wolf and Bleuler (1946) have summarized the findings in respect of endocrine type and personality. Infantilism, virilism in the female, fat dysplasia, an acromegaloid type of habitus, have all been found to run in families in a way which strongly suggests genetical factors. Correlated with physical infantilism tends to go a general childishness of character as well as some retardation of intelligence. With virilism are often associated a lack of femininity of temperament, masculine traits, even homosexuality. The subjects of fat dysplasia tend to be phlegmatic, receptive personalities; and the acromegaloid tend to show features which suggest inadequate control of mid-brain functions. Actual nervous illness may depend more on a dysharmony than on an endocrinological deviation;

for instance, the woman who combines a physical virilism with a soft and feminine temperament is more likely to become nervously upset than the woman who is as virile mentally as she is physically. Wolf and Bleuler ask the question why it is that a quality is now inherited as a unity, now in a fragmentary way as a mosaic? The acromegaloid traits—great height, large hands and feet large lower jaw, large nose and ears—in some families seem to go together, in others to be shown individually and separately by different relatives.

A similar problem has apparently been discussed by Conrad (1941), in a book not accessible to the reviewer. Conrad's views have been criticized by Weissenfeld (1942). According to Weissenfeld, Conrad finds it difficult to explain how both a given physique and a given temperament should go together, being apparently inherited as a unity; it would be unlikely, if many genes were involved, for them all to be situated on the same chromosome; the most probable explanation would be a determination of the character by multiple allelomorphs at the same locus. If this is a correct representation of Conrad's views, the problem has been misconceived. In view of the work of Sheldon, and of Rees and Eysenck, not to speak of *a priori* probabilities, the whole hypothesis of types can be discarded. We must assume that both variation in temperament and in habitus are continuous and, as far as they are genetically caused, attributable to multifactorial genes. This point has been put by the reviewer elsewhere (Slater, 1948). We may, however, assume that a particular physical make-up will carry with it a tendency to show certain temperamental traits, and that, for instance, an endomorphic individual will tend to be viscerotonic as a direct consequence of his endomorphy. Inheritance by multifactorial genes would also seem to be the most probable solution of the problem which Wolf and Bleuler raise in connection with the acromegaloid habitus.

CAPILLARY INVESTIGATION.

Ever since Lombard (1911) first employed the finger-nail fold to observe capillaries in the living subject, and Parrisius (1921) described nail-fold capillary abnormalities in "vasoneurotic" patients, a growing, if sporadic, literature has been produced around this constitutional investigation of psychiatric subjects (de Moragas, 1944). As examples of previous work in this field, nail-fold capillary studies have been made on mental defectives, cretins and cases of juvenile myxoedema, children with enuresis, cases of "traumatic neurosis" and epilepsy, as well as many careful studies on twins between 1925 and 1937, which show that the nail-fold capillary morphology of identical twins reveals a much closer identity to each other than that of binovular twins. While doubted by some workers, it seems reasonably certain that once normal capillary maturation is completed (sometime between the age of six months and eight years), the vascular pattern does not change essentially throughout life. So long, however, as the pattern remains undifferentiated, further development is capable of occurring even up to quite an advanced chronological age. This has been demonstrated very prettily in the capillary maturation of patients suffering from myxoedema who were examined both before and after their treatment with thyroid (Leader, 1932). Jaensch (1929) illustrates in his book the various stages of capillary development.

In the period under review, efforts have been made to employ the simple technique (Davis, 1946) of the visualization of these nail-fold capillaries for the purpose of differentiating between *epileptic* subjects who are likely to deteriorate and those epileptics who, despite continued convulsions, show few or no personality changes or intellectual deterioration (Paskind and Brown, 1943). Normal hairpin forms were found three times as frequently in 100 non-deteriorating epileptics as in 78 deteriorated patients, while the latter also had a higher proportion of bizarre patterns. The authors claim that these capillaroscopic differences afford further evidence of inborn genotypic characters and support their contention that these two groups of patients with epilepsy differ in a fundamentally constitutional fashion.

Hauptmann (1945, 1946) also studied a series of patients with epilepsy, and showed that, of 117 patients, 50 of 73 with idiopathic epilepsy had an "immature" capillary pattern in the nail-fold with horizontal vessels in the proximal part of the area examined, whereas only 10 out of 44 subjects with "symptomatic" epilepsy had this abnormality. A similar immature pattern was observed by Hauptmann in 54 per cent. of 37 patients with *migraine*—a thought-provoking addition to our knowledge of the several ways in which these two conditions resemble one another. Redisch and Pelzer (1943) observed the capillaroscopic changes in migrainous patients in the course of treating them with ergotamine tartrate.

Capillary morphology in *neurotics* has been studied by F. Deutsch (1945), by Hauptmann (1945, 1946) and by Cobb, Cohen and Badel (1946). Hauptmann, for example, noted that of 304 "constitutional" neurotics 268 had an abnormal capillary morphology, whereas only 3 of 71 persons with "neurotic reactions," and 7 per cent. of 125 "normal" controls showed such abnormalities. Irregularities, tortuosity and immature forms were the main characteristics common to constitutional neurotics—a finding closely paralleled by Cobb, Cohen and Badel in 48 cases of patients with *anxiety states*. Hauptmann believes that these findings support the hypothesis that a developmental defect exists in patients with constitutional neurosis, but Cobb *et al.* are not convinced that such capillary patterns represent an unchanging *anlage* of the constitution, holding it unproven that the morphology visualized may not be determined by environmental situations and intercurrent disease. It is obviously desirable that this fundamental point should be investigated so as to put the matter beyond doubt.

Olkon (1945) gives an account of an extensive study of patients with *schizophrenia*. His technique differs from that of other workers in this field in that he employed the area of loose skin between the thumb and index finger. His book refers to a capillaroscopic examination of 1,100 schizophrenic patients, the main deviations from his normal comma-shaped form, seen in 1,056 controls, being a reduction in size and number of capillaries per field, pale colour, lack of uniformity, bizarre forms and the occurrence of haemorrhages. Olkon comments on the prognostic implications of his study and states that capillary disorganization progresses as the disease advances—a claim contested by other workers. In the same book, Olkon mentions capillary investigations in cases of *manic-depressive psychosis*, noting in specific case-histories abnormalities

such as spasm, irregular distribution, sparseness and sclerosis of the vessel walls.

The foregoing investigations represent, in the main, careful research in the descriptive sphere of capillary microscopy. It will be obvious, of course, that much work remains to be done. Confirmation of the above work is awaited, capillary studies on many psychiatric conditions remain still to be reported on, and exact correlations with physique, prognosis, the effect of treatment and with biochemical and other pathological investigations, are but a few of the rewarding problems to be tackled. In addition it is still conjectural as to what is the significance of finger-nail fold capillary morphology for the neurophysiology of the central nervous system. Jaensch (1929) believed that capillary differentiation proceeded in step with the degree of myelination of the C.N.S. This belief, however, remains pure speculation, and even were it ever proved, the findings of Romanes (1947) would suggest that it is of little relevance. Far more to the point would seem to be a study of the possible correlation of finger-nail fold capillary patterns with those of the cerebral capillary formations.

ENDOGENOUS PSYCHOSES.

The whole theory that heredity plays any part in the "functional psychoses" has been attacked by Rosenberg (1944). He points out that the mere recurrence of a morbid condition in a family history is no *proof* of heredity, and cites as an instance to the contrary the scrofulous diathesis. It is unfortunate for his case that the theory that hereditary factors play an important part in susceptibility to tuberculosis is a well established one, and has recently been strikingly confirmed by the twin investigations of Kallmann and Reisner (1943). Twin studies are, however, dismissed by the comment "obviously heredity cannot produce schizophrenia in one twin and not in the other." All our hard-won knowledge has no meaning because "to the modern psychiatrist, generation after generation of insanity means schizoid or manic parents imposing their unreasonable attitudes on children who warp under the family tensions."

A similar inspiration underlies the work of Gralnick (1943). He describes an interesting family of father, mother, son and daughter. The mother, presumably a chronic paranoid schizophrenic, completely dominated her family and forced them to live an isolated existence in dirty and deteriorated conditions. The father became psychotic at 62, paranoid and hallucinated. The son died of malnutrition at 18 without any definite mental illness; the daughter developed disseminated sclerosis and a paranoid reaction. The illnesses of father, son and daughter are interpreted as the result of "sociogenesis," and not "biogenesis"; the psychosis of the mother proves inexplicable on these principles, and is not discussed. The author remarks that "many cases of *folie à deux* have been reported in the literature, but none in this detail." It is a pity that the detail is insufficient to allow an independent clinical judgment of the case material. Other psychotic families have been described by Sutter (1942) and Osborn (1945). The family described by Sutter, with seven mentally affected members, is described in terms of the French nomenclature, and is interesting for the attempt the author makes to dis-

entangle the induced and the endogenous elements. Osborn's five psychotic sisters were all schizophrenic, but repeatedly diagnosed in hospital as manic-depressives.

Kallmann and Mickey (1946) criticize too wide a use of the term *folie à deux*, and, discussing the possibility of an explanation of familial psychoses by induction, point out how inadequate this explanation often is. Among the instances they quote is that of a family with a schizophrenic mother, a possibly schizophrenic father, and seven schizophrenic children, all of whose psychoses occurred in wide isolation from the others. "Poor environment, intimate contact and suggestibility are not sufficient to produce an accumulation of manic-depressive or schizophrenic psychoses in certain family units." "Similar delusional syndromes should not be called 'induced,' or *folie à deux*, if they appear in units of blood relatives, and if the primary significance of the factor of blood relationship cannot be safely excluded." The rarity of suicide in twin pairs has been emphasized by Kallmann and Anastasio (1946, 1947). In a search of the literature they were unable to find a single pair in which both twins had taken their lives. They are inclined to think that this is not accidental, and that if one twin commits suicide the other is thereby to some extent protected against suicide, perhaps by the existence of a rivalry situation.

Penrose (1945) has published interesting figures based on 5,456 related pairs from mental hospital admission registers; the material has so far been published only in abstracted form. Results show that schizophrenia, affective psychoses, senile psychoses, etc., tend to run true to type, but that schizophrenic and affective psychoses are not very distinct. Figures indicate that sex-linked genes play some part in determining age of onset.

Myerson (1946) has discussed the data provided by the family histories of patients seen in a private consultative practice. In epilepsy and mental defect the family history was nearly always negative; but it was positive in 47 per cent. of the manic-depressive patients, in 23 per cent. of the schizophrenics, and 12-15 per cent. of the neurotic and psychopathic patients. This last finding seems remarkably low. Lang (1945*b*) investigated the families of Jewish refugees from Nazi oppression, a total of 1,630 relatives of 80 *propositi*. The frequency of mental defect, epilepsy and schizophrenia was less than expectation, and only manic-depressive states were in excess. He concludes that, as a result of its curious system of eugenic values, the Nazi régime drove out a positive rather than a negative selection. Schulz (1942) has contributed a useful clarification of the statistical technique of calculating the correction for age in a population investigated for the frequency of conditions which come on during the course of life; and Shrimpton and Slater (1939) have published a technique, provided by Irwin, for the calculation of the standard error of Weinberg's morbidity table. Hurst (1944) has discussed, for a general medical audience, the present standing of genetics in psychiatry, with some original case material.

The present standing of genetics in the theory of the endogenous psychoses has also been discussed by Bleuler (1942, 1948*a*). He considers that the achievements made by psychiatric genetics must be regarded as very modest; Mendelism, so to speak, has failed. He is, however, over-pessimistic, especially

in holding that the genetics of mental deficiency do not now stand on a very firm and satisfactory foundation. The concept of multifactorial inheritance is apparently unfamiliar on the continent. Due regard, Bleuler says, has to be paid to the results of empirical study (*empirische Erbprognose*), but this is not much on which to congratulate ourselves. A more promising outlook is promised by clinical-genetical analysis (*Erbanalyse*). Enquiries along this line have led to a clarification of our views about idiopathic and symptomatic epilepsy. Similar advances have been made in schizophrenia. Personality deterioration loses the central position assigned to it originally by Kraepelin; it is not the feature in which affected relatives most closely resemble one another (as it is in the case of epilepsy). Heredity analysis confirms the distinction drawn between schizophrenia and organic disorders, but not that between schizophrenic and affective ones (see also Penrose, above). The physical methods of treatment may provide us with new modes of classification (see Siegfried, below), a point which was also made by Myerson (1946). The "*Ganzheite*," the wholes or entities, with which psychiatry operates, are not entirely suitable subjects for the geneticist. Quite new lines of advance may be opened by animal pathology and animal experiment (see Grueneberg, above), by psychotherapy and the developments of Freudian doctrine. Psychoanalytic theory is now transferring the emphasis from infantile experience to long-lasting conflict situations; these conflicts may find their basis in dysharmonies of genetical make-up (as in the case of virilism, noted above). We must take account of conflicts not only between the individual and the environment, but also within the individual himself.

WORK ON TWINS.

A highly interesting observation, with implications for the theory on which twin work is based, has been reported by Zlotnikoff (1945). This was that of a human mosaic. The patient, a woman, showed a pigmented naevus almost covering the left side, and confined strictly by the mid-line. The right iris was grey, the left dark brown; the left side of the head was bald; and the left side of the body sweated more abundantly than the right. The author suggests a somatic mutation at the 2-blastomere stage. Mosaics are known in other species; and it has always been appreciated that it is theoretically possible for a somatic mutation to occur which would cause a single gene difference between two otherwise identical twins. This, however, is the first relevant observation on a human being, unless the occasionally observed case of anisochromiridia is accepted in this sense, which is not conceded by Dahlberg (1942). Dahlberg would regard such relatively trifling differences as a manifestation of asymmetry, and not due to genetic differences. In this paper Dahlberg discusses the validity of the argument, very commonly used, that any respect in which uniovular twins are more concordant than binovular ones must depend on genetical factors. He shows that the relative proportion of concordance and discordance depend, *inter alia*, on mode of inheritance and gene frequency.

Another point of theoretical importance has been discussed along mathematical lines by Rosin (1947), namely, the possible existence of oocytic twins.

If they occurred, these twins might be a half-way stage between uniovular and binovular twins, being derived from the fertilization of a polar body. Oocytic twins could, however, only have a greater similarity than binovular twins in the case of pre-reduction; in the case of post-reduction they would be less alike. Over a series of twins, therefore, this possible source of confusion may be neglected; and, in general, the assumption can still be maintained that binovular twins will share on the average the half of their genes. Rosin points out that the existence and the frequency of oocytic twins could be discovered by investigating the twin children of crossings in which the mother was heterozygotic for a dominant, the father being homozygotically recessive. Serological studies would seem to be the obvious source of such a material. A contribution to the statistical methods which may be applied to twin data has been given by Schinz (1945).

Individual case studies of uniovular twin pairs have been provided by many authors. Adler and Magruder (1946) describe a pair of female schizophrenics with *folie à deux*; the more dominant sister developed symptoms a few hours before her twin, and in the latter the psychosis was thought to be induced. Nevertheless, she failed to get better of her own when her twin recovered after E.C.T., and failed to respond until treated in the same way herself. In her case treatment was begun 17 days later and produced a slightly less satisfactory result, suggesting the advisability of early treatment. A rather similar pair in which psychological induction may have played some part is described by Laignel-Lavastine and Bendit (1940). Concordant schizophrenic pairs, though without points of special interest, are described by Rubin (1944), Stolze (1942), a case of concordant symptomatic psychosis by Grosch (1944), and one of an intractable depressive tension state with depersonalization by Palmer (1946). Craike and Slater (1945) describe a concordant pair with paranoid schizophrenia, whose special interest is that they were separated in infancy and developed apart, yet each eventually suffered from delusions in which the other was involved. Elste (1941) reports a case in which character development in the two twins seemed to occur in opposite directions, and considers that such psychological "polarities" may explain some discordances in uniovular twins. Arieti (1944) reports a pair of schizophrenics of whom one made a spontaneous recovery, while the state of the other remained unchanged. The patient who recovered was the more athletic in habitus, had a more extraverted personality, better social adaptation and, in the psychosis, a more atypical symptomatology. The author suggests that the antischizophrenic defence mechanisms, postulated by Kallmann and his co-workers, may show themselves at the psychological level in atypical symptoms.

Twin work of a more systematic kind and on a large scale has been reported in psychopathy, epilepsy and schizophrenia. The work of Rosanoff, Handy and Plesssett (1941) on childhood behaviour disorders, and juvenile and adult delinquency was accessible to the present reviewer only through the medium of a review. In this monograph 409 case records are published *in toto*. In 137 uniovular twin pairs, in only 18 cases was one member only of the pair delinquent or disordered. In 272 sets of fraternal twins this was true in 170 cases. The difference is very striking. Males were much more frequently affected than

females. The authors emphasize the significance of environmental factors (!), especially of brain trauma.

The work of Lennox and his co-workers has been reported in four publications. The brain-wave pattern is shown to be to a large extent hereditarily determined. In 55 uniovular pairs the EEG tracings were identical in 85 per cent., unlike in 95 per cent. in binovular pairs (Lennox, Gibbs and Gibbs, 1945). Rather less satisfactory is the work on the relation between epilepsy and intelligence (Lennox and Gibbs, 1944; Lennox and Collins, 1945), in which the statistical data are awkwardly handled. The main conclusion is that idiopathic epilepsy does not have any severe effect on the intelligence. Lennox (1947) describes further data from family as well as twin investigations. Familial incidence was found to be higher in cases with an early onset, or without brain lesion, or accompanied by mental defect. The EEG's of 470 near relatives are also reported. In epileptic twin pairs without brain pathology there was 94 per cent. concordance in the uniovular pairs, 17 per cent. in the binovular pairs with brain pathology, and only one of the binovular pairs was concordant.

The work of Essen-Moeller on psychotic, mainly schizophrenic, twins (1941) is remarkable for providing complete case histories of all the uniovular pairs. This sets the material on record, if need be, for critical analysis by another hand at a later date, when the further advance of knowledge may perhaps suggest re-examination with other ideas in mind. Starting from a psychiatric population of 8,586 patients, Essen-Moeller found 71 twin pairs, of which 21 were uniovular. In the 7 schizophrenic pairs, 5 of the co-twins had psychoses, but none of them typical schizophrenias. There were considerable concordances in mode of precipitation, degree of periodicity, and amount of schizophrenic disorder of thought and perception; age onset, outcome and affective symptoms showed rather marked quantitative differences. Psychogenic factors of significance could not be isolated by the investigation; the main possibly causative environmental differences were of a physical nature, hormonal, pregnancy, head trauma, birth injury, tuberculosis. The author comments: "Process-type schizophrenias are matched by transitory psychoses, not leading to defect, and by partly reactive psychoses. . . . It is genetically significant whether schizophrenic symptoms were present, less so whether the course was mild or severe" (see also Bleuler, 1941). In regard to character-ology, he says: "Those anomalies with some connection to the endogenous psychoses seem to be, much more than the psychoses themselves, dependent on the *anlage*. . . . From the genetical and aetiological standpoint it is not so important to distinguish between a psychosis and its corresponding psychopathy, as to distinguish the psychopathies from each other and from the normal."

Findings very different from the statistical point of view, have been made by Kallmann and his co-workers (Kallmann, 1946*b*). From a resident population of 73,252, and 12,316 new admissions, 794 schizophrenic twin index cases were discovered—an almost astronomical number by ordinary standards. The families of all members were also investigated. The incidence of schizophrenia among uniovular co-twins was 86 per cent., among binovular twins 14 per cent. In uniovular twins who had been separated for 5 years before the onset of the

psychosis in the index case, the incidence in the co-twin was a little lower, 78 per cent. No evidence of any causal influence from birth difficulties or from handedness was found. Environmental differences generally exerted no large influence. There were considerable differences in age of onset, and in nearly 30 per cent. of concordant uniovular pairs there was a difference of 4 years or over. The concordant uniovular pairs were much more alike than the concordant binovular ones in respect of degree of deterioration suffered. The author believes his findings, of which no more than a selection are mentioned here, support the theory of a specific recessive autosomal genetical factor as responsible for the predisposition to the disease, with a multifactorial determination of constitutional powers of resistance, to which considerable significance is attached.

Such a large case material could hardly be published in full, although very large and detailed case collections have recently been published in the States. Illustrative case material from this gigantic collection has, however, been published by Kallmann (1948*b*), and Kallmann and Barrera (1942). Further theoretical considerations, based on this material, are also given (Kallmann, 1948*c*, 1948*d*). The paper by Kallmann and Barrera is interesting for giving further statistics relevant to the problem of constitutional powers of resistance. The work consisted in the application to hospitalized schizophrenics of the Sheldon scheme of body typing. The athletic component was found to be much weaker in deteriorated schizophrenics, much stronger in the best preserved. In twin material Kallmann believes it is a general rule that the illness comes on sooner, or takes a more malignant course, in the twin who is behind the other in growth, weight, height and physical strength.

SCHIZOPHRENIA.

Important work on the relation between schizophrenia and endocrinological variations has been carried out by Bleuler and many collaborators and students of his school (Barich, 1946; Kaufmann, 1943; Ott-Schaub, 1943; Sorg, 1945; Stockmann, 1946; Sulzer, 1943; Wander-Voegelin, 1945; Wolf, 1946). The programme was laid down in advance (Bleuler, 1943), and carried to a successful though provisional conclusion. In a monograph by Bleuler (1948*b*) and eight collaborators, which occupies a special number of the journal in which it is published, the whole of the conclusions are described and debated with a wealth of clinical material. Early in the work programme Mueller (1944) published a critical review, with over 400 references, of all previous work on the subject. This review gives a survey of the psychiatric disturbances which have been observed in the disorders of the thyroid, hypophysis and sex glands, in diabetes and with insulin, in tetany, Addison's disease, osteomalacia and polyglandular endocrinopathies. Observations on endocrine anomalies observed in schizophrenia are also reviewed. This work should be of great value.

The goal which Bleuler set himself and his collaborators was the ascertainment of schizophrenic patients with some endocrine abnormality, and then by the investigation of other members of their families the analysis of pathogenetic or pathoplastic relations between the two kinds of abnormality. Patients were

found with an acromegaloid habitus, i.e. not suffering from acromegaly (which appears to be a completely distinct condition and without a genetical basis), but showing such features as great height, large hands, feet, jaw and nose, etc. This type of bodily make-up was associated with psychological peculiarities—periodic swings of mood into depression, irritability, etc., periodic exaggerations of the sexual urge, polyphagia and poriomania. This type of psychosomatic constitution was strongly hereditary and behaved in the affected families in many ways like a dominant. Furthermore, these families showed an excess of schizophrenia, and the combination of schizophrenia with an acromegaloid constitution was unduly frequent. The symptomatology of the schizophrenic psychosis, when it occurred in an acromegaloid, was not essentially different from the usual picture, but onset tended to be late, the course mild, and deterioration less extreme. Other investigations in Cushing's disease, virilism, fat dysplasia, infantilism and Simmonds' disease, showed no enhanced tendency of sufferers from these conditions to develop schizophrenia; excessive obesity, virilism and infantilism were found to depend on genetical factors, and these conditions exerted some pathoplastic effect on the symptomatology of a co-existent schizophrenia. The psychiatric abnormalities associated with Cushing's disease and with Simmonds' disease were non-schizophrenic.

Control material for these investigations was provided by earlier investigations of Bleuler (1941), which are important in themselves. The *propositi* consisted of 100 schizophrenics in the U.S.A. and 100 in Switzerland. In the U.S.A. 2,634 relatives were investigated, in Switzerland 8,776. Family loading was heavier in the Swiss than in the American material, but agreed with the findings of previous investigators. Valuable statistics, for control purposes, are provided about the relative frequency of different types of previous personality, course, end-state, etc., and about their mutual interrelations. The incidence of schizophrenia in the relatives of subgroups of schizophrenics showed no significant differences when the *propositi* were classified by previous personality and by end-state, though the patients who recovered had a slightly higher family incidence; it was the patients without a family loading who tended to fall ill earlier and to run a more serious course. This finding, statistically not well established, suggests, of course, some heterogeneity, recessive factors being associated with greater malignancy. Comparing related schizophrenics, family resemblances were striking in respect of previous personality, age of onset, course and end-state, though Bleuler does not make use of the most efficient tests of significance, and so is inclined to think his findings less important than they are.

A statistical examination (Slater, 1947a) of the case reports of 92 schizophrenic sibs, published by Zehnder, lends support to Bleuler's findings; this investigation showed that age of onset, Kraepelinian type, course and outcome, degree of affective dilapidation, presence of catatonic signs, prominence of affective and paranoid symptoms, were all more alike in pairs of sibs than chance would allow. The theory is proposed that multifactorial genes are responsible for these resemblances. The work suffers from the fact that it was not done at first hand. In this material the correlation coefficient between ages of onset in schizophrenic sibs was found to be 0.55. Stroemgren, on less

highly selected material, found one of 0.19, and Schulz (1940*b*) between schizophrenic parents and children, one of 0.27-0.37.

Genetical work of direct applicability in the problems of treatment, and inspired by Bleuler's line of thought, is reported by Siegfried (1942). The families of 90 schizophrenics who had proved resistant to shock therapy were investigated. Catamnesis showed that in 80-90 per cent. the course was uniformly progressive, and the outlook had therefore, probably from the beginning, been bad. The families of these patients showed a lower loading than in control groups, once more suggesting that recessive genes were involved.

Looking at the above work as a whole, one may say that this renewed attempt to break up the probably heterogeneous group of the schizophrenias into genetical subgroups is promising, but has not got very far. So far, most of the differences found between subgroups could be attributed to non-specific multifactorial genes. Bleuler (1947) discusses these problems in some detail. He points out that in some families schizophrenia seems to go with a schizoid personality, in others with a normal personality, or with a hysterical or obsessional one. In some families particular sorts of psychogenesis seem to be necessary before the psychosis breaks out, or there are associations with alcoholism, or endocrinopathy. The very diagnosis of schizophrenia is difficult; and though we have certain means of distinguishing schizophrenic from any organic form of disorder, the differentiation from affective states never enjoys quite the same certainty.

Schulz also is inclined to suspect that there are genetical factors common to both schizophrenic and affective disorders. His earlier figures were discussed in a previous review (Slater, 1944*a*). Later papers, not then available, may be mentioned. In the children of 31 matings between schizophrenic parents (Schulz, 1940*a*), there were 38 per cent. of schizophrenics, 45 per cent. if dubious cases were allowed. The incidence of manic-depressive disorder was negligible. Schulz considers that the rise in the incidence of schizophrenia from 10-15 per cent. among the children of one schizophrenic to 40 per cent. among the children of two schizophrenics, is against the theory of dominance proposed by Koller. In a total of 55 sibships resulting from the mating of two manic-depressive parents (Schulz, 1940*c*), the incidence of affective psychoses in the children was 28 per cent., of schizophrenia 12 per cent. The high incidence of schizophrenia suggests a common genetical factor. In 30 sibships resulting from the mating of one manic-depressive and one schizophrenic parent (Schulz, 1940*d*), the corresponding figures were 24 per cent. and 8 per cent.—lower than in either of the other two types of crossing. Schulz proposes the theory that there is a gene for endogenous psychosis, which may be either affective or schizophrenic, and an additional gene which determines the form, but which by itself leads to no psychosis. The theory is not an aprioristically probable one.

Another attempt, derived from the school of Kleist, to break up schizophrenia into smaller and more homogeneous subgroups, has been made by Leonhard (1942*a, b*, 1943*a, b*, 1944*a, b*). The attempt consists very largely in a refined clinical analysis, but also in family investigations which show that the incidence of schizophrenia is much lower in the families of "typical"

than in the families of "atypical" schizophrenics, the latter being the paranoid, confused and periodic types. Leonhard, for instance, found 22 per cent. of schizophrenics among the sibs of periodic patients, only 5 per cent. among the sibs of typical cases. A strictly controlled experiment was carried out by Schulz (Schulz and Leonhard, 1940) on this basis. While Leonhard diagnosed the cases, Schulz investigated the families; each were in ignorance of the decisions being formed by the other. Leonhard's point was sustained, though not conclusively; comparing typical and atypical cases, the incidences in sibs were, respectively, 6 per cent. and 8 per cent., in parents 1 per cent. and 6 per cent. Further confirmation of Leonhard's view is given by the work of Edelmann (1942). Once again the suggestion of a differential incidence of recessive and dominant genes arises. This work is interesting, and represents to some extent a triumph of clinical psychiatry; but the differences between "typical" and "atypical" are too subtle, and probably too liable to error, to make such a clinical differentiation a satisfactory basis for research. Very few investigators could expect to have Leonhard's acumen and experience, or to be able to rely on documentary material of the same merit.

Other investigations are of less interest. Egger (1942) and Frueh (1943) confirmed Leistenschneider in showing that there is only a very slight excess of schizophrenics among the consorts of schizophrenics and their families, and that there is therefore no high rate of assortative mating in respect of a schizophrenic gene. This is of importance to the theory of recessivity. A study of the fertility of schizophrenics and related themes is provided by Jordans (1941). Formanek (1942) has discussed the work of Bleuler (1941). Stancu, Clark and Snyder (1947) have found that the blood of 75 schizophrenics and their mothers showed no excess of Rh incompatibility. Barahal (1945) has given some arguments which support the theory of recessivity in schizophrenia. Bellak and Willson (1947) assert that heredity is of no significance in the aetiology of schizophrenia; the disease is psychogenic. Weinberg and Lobstein (1943), working with a Jewish population, have found that consanguinity rates among the parents of schizophrenics are much higher than in their parallel investigation of affective psychoses (14 per cent. : 6 per cent.); they provide statistics on familial incidence in subgroups which are not very striking. Hoch (1943) has found that there was no excess of epilepsy among the sibs of schizophrenics, and in general no indication of any genetical connection between the two conditions. Some epileptic psychoses were, however, very difficult to distinguish from schizophrenic ones.

AFFECTIVE PSYCHOSES.

The important work of Schulz has already been mentioned. Careful work has been done by Becker (1942) on a single family of 110 healthy and 68 psychiatrically abnormal persons. From the starting sibship the mother's line shows typical manic-depressive mood swings and manic-depressive psychoses without any atypicality. Occasional neurasthenic and reactive pictures are seen. The father and his relatives show no psychoses and no sign of a cyclothymic component, but instead the occurrence of abnormal personalities, sensitive, pedantic and scrupulous. Where these two trends blend temperaments

of mixed kinds are found, and atypical psychoses, e.g. affective psychoses with an anankastic colouring. Becker thinks that the manic-depressive genotype can activate other, e.g. schizophrenic, tendencies. The essential expression of the thymopathic *anlage* is the mood swing itself. The case records are given in commendable detail.

Work on involutional and climacteric depression has been done by Bischof (1939), Brockhausen (1939) and Majer (1941). Brockhausen's paper, a few lines only, mentions a material derived from 201 female cases, and states that his earlier findings on 31 families are fully confirmed. The single involutional illness, without a phasic quality, is genetically distinct from manic-depressive psychoses. On a small material Majer finds that while there is a heavy incidence of affective disorders among the relatives of involutional and climacteric depressives, the incidence among the relatives of reactive depressives was almost negligible. Bischof, on a material derived from 109 female patients, found an extremely low incidence of psychosis among the sibs of the climacteric patients (2 per cent.) in contrast with a 14 per cent. incidence among the sibs of involutional cases. He thinks that the hereditary factor may be negligible in climacteric depressions.

Burkhardt (1942) has reported an investigation into the incidence of manic-depressive disorders in Schleswig-Holstein, and found it to be very low—only 2.6 per cent. of hospital admissions. Really typical pictures were extremely rare.

EPILEPSY.

The work of Lennox and of Hoch has already been mentioned. Franke (1945) has reported a family in which both mother and son showed a combination of optic neuritis (Leber's disease) with epileptic equivalents; and Gallot (1940) a family in which epileptics continued to appear over 4 generations, a total of 11 males and one female being involved. Snyder and Palmer (1943) have reported a family, derived from a rare religious group addicted to inbreeding, in which a convulsive disorder could be attributed to a partially sex-linked gene (though an autosomal recessive could not be excluded); the condition appeared about the age of one and caused death in a state of advanced dementia between 4 and 12.

An interesting argument, capable of wider application, is advanced by Schulz (1941). The factual data are supplied by the researches of Conrad. Among the children of 306 epileptics Conrad found 6.9 per cent. of epileptics. Schulz, using this incidence rate, calculates the expected number of sibships with 1, 2, 3, etc., epileptics. He shows that 50 sibships with an epileptic could have been expected, but only 45 were found, i.e. some sibships were too heavily loaded. If *a priori* methods are applied to the families with at least one epileptic, the frequency of epilepsy rises from 5.5 per cent. to 15 per cent. Two explanations are possible: either the *propositi* were not homogeneous genetically, or their consorts were not, and some were incapable of procreating an epileptic child. If the expectation of epilepsy is p , then in a sibship of n persons the probability of there being no epileptic is $(1 - p)^n$. In this way, given the numbers of each sibship of stated n who have an epileptic, one can calculate how many more

sibships of the same n should, by chance, have had no epileptic. For the 45 epileptic-containing sibships there would be an additional 99 who, by chance, produced no epileptic. The sum of these two, 136, is only 40 per cent. of the total material of 337 sibships. A similar result is obtained when examining the same families for the incidence of mental defect. Furthermore, similar results were previously obtained on other material with schizophrenia. In every case there is an indication that a considerable proportion of the consorts of epileptics, schizophrenics, defectives, are incapable of procreating children with the abnormality in question.

ORGANIC PSYCHOSES.

Essen-Moeller (1946b) has described a case of Alzheimer's disease with pathological findings; a brother and mother were also affected, and the prevailing impression that this disease depends on a dominant gene receives support. Worster-Drought, Greenfield and McMenemey (1944) have described a familial presenile dementia with ataxia and progressive spastic paralysis, but the report is largely pathological, and genetical findings are not enlarged on. Other families with cortical atrophy, e.g. especially Pick's disease, are described by Bebin and Paredes (1947), Friedrich (1940), Malamud and Waggoner (1943), Mallison (1947). In most of these papers the main interest is pathological, but details about the families are given in every case, sometimes extensively, and in every case are in conformity with simple autosomal dominance. Jéquier (1945) has reported in great genealogical and clinical detail 8 families with Huntington's chorea. The results obtained lie in some greater precision on both the clinical and pathological side; but the opportunity was not taken to analyse familial resemblances in the clinical picture, or to show how the clinical picture varied, if it does, with age of onset, etc. The material is reported in sufficient detail for further work on it to be possible. With such extensive genealogical work being done, it was a pity that another opportunity was missed, that of making linkage studies.

The same remark applies, though in the case of recessive abnormalities linkage work is more difficult, to Sjögren's very large collection of families with hereditary ataxia. This work is of psychiatric interest because of the occurrence of psychotic states late in the course of the disease. Contributions to the psychiatry of the hereditary ataxias have also been made by Bleuler and Walder (1946), Schneider (1946) and Bloechlinger (1946). Their findings, which are all in agreement, are that late in the disease a deterioration of personality supervenes which is indistinguishable from the epileptic alteration of personality, although epileptic fits are very unusual. There are the same egocentricity, the same religiosity; affect is superficial, thought is controlled by affect, there is poverty of ideas, and ideas lose their sharpness. There is little disturbance of memory, but often some retardation. Frankly psychotic pictures occur and then take a characteristically organic form, with delusional ideas and hallucinations in the foreground. The hallucinations resemble those of the epileptic twilight state, in their affective tone and scenic quality. Psychiatric disturbances in dystrophia myotonica have also been recently described (Stolba, 1947). A constitutional factor in Sydenham's chorea is

suggested by recent research. Krauss (1946) confirms Guttman's finding that in the families of choreics there is not only an excess of chorea but also an excess of schizophrenia, especially of catatonic type. Lewis and Minski (1935) have reported that the rare choreic psychosis has a marked clinical resemblance to schizophrenia. Usher and Jasper (1941) found an excess of EEG abnormality among the non-choreic relatives of choreics.

The rarely observed curiosity, *hyperostosis frontalis interna*, which has attracted psychiatric attention, was subjected to systematic investigation by Grollman and Rousseau (1944), 42 patients being studied. They conclude that the condition is inherited as a dominant, is relatively common, is combined with endocrine disturbances, obesity, hirsuties, hypertension, but is associated with no characteristic psychiatric picture.

A general theory accounting for the occurrence of senescence on a genetical basis has been given by Medawar (1946), but is described in the review on "Problems of Ageing" in this volume. The theory is so convincing that it becomes a puzzle to account for the existence of species in which senescence does not occur.

NEUROSIS AND PSYCHOPATHY.

The constitutional basis of neurotic illness and its relation to psychopathic personality attracted the attention of British psychiatrists generally during the past war. Much work was done with men who broke down under the stress of enemy action or of other strains accompanying the war situation; and psychiatrists generally agreed that not every man was equally liable to break down, and that the whole of the differences between individuals could not be accounted for by differences in the degree or nature of the strains imposed. This view was accepted also by many who still regarded the psychological aspects as prepotent and attributed differences in susceptibility to stress to factors in Oedipus development, to differences in the infantile psychological traumata suffered, etc. A genetical basis for this constitutional variation was, however, also important. The work of Eysenck (1947) showed that neurotic individuals differed from normals both in physique and in temperamental make-up; and Symonds (1943) showed that the liability to breakdown varied inversely with the loading with signs of life-long instability. The work of the present reviewer is of some theoretical importance in connection with the genetical factor.

A statistical study of two thousand neurotic soldiers (Slater, 1943) had the following as its main conclusions. Neurotic breakdown was the product of the interaction of two variables, constitutional predisposition on the one side and a factor of stress on the other. Both of these variables should be considered quantitatively. The reaction, when it occurred, tended to follow the pattern of behaviour usual to the individual concerned; and its form was determined more obviously by the past personality than by the nature of the stress undergone. The reaction itself was of a rather unspecific nature, and usually consisted in a mixture of various possible modes, anxious, hysterical, depressive, etc. A factor analysis showed that a very substantial proportion of the total variance could be accounted for by two factors, "neurotic con-

stitution" and "inadequate intelligence." The parallelism between intelligence and temperament was emphasized. The argument was taken a step further by Slater and Slater (1945). The existence of a genetical basis for the tendency to neurosis was regarded as established by such findings as a high incidence of psychiatric abnormality in the first-degree relatives of neurotics, and the work of others in demonstrating great similarity of personalities in uniovular twins, etc. Various theories of the nature of the genetical basis are discussed, and the conclusion is reached that this is of a multifactorial type and determines variation in a number of dimensions. In favour of the theory it could be claimed that it accounted for the apparent qualitative difference between the neurotic and normal, for the finding that neurotics fall within the range of normal variation in any quality in which they are measured, the finding that the frequency of breakdown varies with the intensity of the stresses imposed, that certain types of stress are liable to produce breakdown among particular types of personality, that mixtures of characteristics, and therefore mixtures of symptoms, occur among neurotics more frequently than do pure states, that neurotics are found to be heterogeneous and more variable than normal controls, that among the relatives of *propositi* suffering from a given type of neurosis the incidence both of the same and of other kinds of neurosis are found to be higher than among the normal population. The theory is presented in a precise mathematical form which permits its consequences to be tested by the usual biometric statistical methods.

Some applications of this theory were later added. Further statistical investigations of the original case material (Slater, 1945) showed that the constitutional predisposition to neurosis was associated with a deficiency in sex life. Various hypothetical explanations of this finding were discussed, and it was thought that a particularly promising line for further investigation would be to seek for the common factors in an endocrine imbalance. The relation between the neurotic constitution and psychopathic personality is further discussed by Slater (1948), and the two are regarded as to a large extent mutually overlapping. The thesis is there advanced that constitution must be a dynamic concept, as a disposition which is constantly altering with time, and is subject not only to the unfolding which is determined by latent genes making their effects manifest, but also to changes caused by environmental influences. The meaninglessness of a purely static concept, even from a purely genetical point of view, is emphasized. The bulk of genetically determined variation should be attributed to multifactorial genes. The similarity between intelligence and temperament, from the biological point of view, is held to suggest that deviations from normality in the distribution of temperamental gradings might be accounted for by pathological genes and environmentally determined pathology, e.g. in such psychiatric conditions as post-traumatic personality change, the schizoid personality, etc.

Slater's views, though developed independently, were in many essentials anticipated years ago by workers whose concepts found little acceptance in British and American psychiatry. Kurt Schneider first formulated the applicability of statistical rather than ideal concepts of normality to the problem of psychopathic personality and held that psychopaths fell within the

normal range. The mathematical formulation, which Schneider's presentation lacked, was itself supplied by Sjoebing, whose work is almost unknown in this country, and whose first publication on the subject appeared in 1913. Essen-Moeller (1946) has recently given an account in English of Sjoebing's ideas. He regarded temperamental traits as distributed in a normal curve, deviations from this curve being caused by pathological agents. Four dimensions of variation are considered, intelligence being one; the temperamental variations are "stability," "solidity" and "validity." At the negative extreme of the first are the substable, the warm, interested in others, extensively active personalities; the superstable are cold, interested in ideas, intensively active. The subsolid are quickly reactive, flexible, subjective; the supersolid are slow, objective, self-possessed. The subvalid are retiring, tense and anxious; the supervalid expressive, venturesome, self-confident. To take one example, the schizoid in Sjoebing's views would be a pathological variant, but the Kretschmerian schizothyme would be describable in terms of superstability and supersolidity. The scheme which Sjoebing advanced has been found very helpful by his Scandinavian students in analysing and describing personalities, and in analysing the structure of psychoses and differentiating the features derived from personality from those derived from disease.

Other work on the genetical basis of neurosis and the personality disorders is of a rather miscellaneous nature. Slater (1947*b*) has shown that an enhanced tendency to neurosis is associated with certain religious groupings; Jews, for instance, had an extremely high neurosis rate, to judge by military casualty rates, but it would be dangerous to explain this solely in the terms of genetically determined racial differences. Leiter (1939), in a rather unsatisfactory paper, attempts to associate asocial behaviour with particular character traits, and describes personality structure in socially difficult children and juveniles which differs in those of normal and those of inadequate intelligence. Among the relatives of the propositi the constellations of personality traits tended to break up and be inherited independently; but there was a high incidence of criminality among the relatives of the affectively cold. Gottlieb, Ashby and Knott (1945, 1947), in two papers hampered by statistical inadequacies and a lack of clinical description, associate "primary behaviour disorders" with an abnormal family history and abnormalities in EEG record. The frequency of an abnormal EEG was greater in those cases with a psychiatrically abnormal family history (as has also been recorded by Liberson and Seguin (1945)) or with a personal history of head injury. EEG results indicated that some of the behaviour problem children might be suffering from pre-clinical epilepsy. In an interesting article on the famous Kallikak family, Scheinfeld (1944) provides a devastating though kindly criticism of the work on which the original publication was based. It will be remembered that the ancestral Kallikak was supposed to have been the progenitor, by one feeble-minded and morally loose mother, of a race of defectives and degenerates, and by a legal union with a Quakeress of good personality and antecedents, the ancestor of a contrasting race of socially admirable individuals.

Hereditary factors in alcoholism are the subject of three communications. That by Lemere *et al.* (1943) shows a family history of alcoholism in 62 per

cent. of alcoholics, in 29 per cent. of psychiatrically abnormal persons who were normal drinkers, and in 16 per cent. of normally-drinking controls. Roe, Burks and Mittelman (1945) followed up the careers of 78 foster children of known parentage; some of these came of normal, others of alcoholic and of psychotic parentage. The results were inconclusive, as although the children of normal parentage excelled the others in various ways, they had, by means which could not easily be explained, also been provided with better foster-homes. An interesting article by Williams (1947) discusses the tendency to addiction to alcohol as being possibly an inborn error of metabolism. He ranges over a large part of the field of the idiosyncrasies, and produces striking positive evidence that alcoholism should be regarded in this light. In his view, both hereditary factors producing the idiosyncrasy, and environmental factors causing the initial consumption of alcohol, would be involved in the production of the addict.

Further work has been added by Lang to his earlier studies on homosexuality, discussed in the previous review (Slater, 1944a). Lang's theory that homosexuals represent an inter-sex was supported by his findings that there was an excess of males among the sibs of male homosexuals. These earlier findings are summarized by Lang (1940). His statistical technique has been criticized by Koller (1942), who points out that the findings could equally well be explained if homosexuality in a male was a quality which could be produced by a *brother*, and that the best test of Lang's theory would be an examination of the sex-ratio in children of homosexuals—male homosexuals should produce an excess of females by this theory. Lang (1942) has replied to these criticisms. He has also (1944) provided some data about hermaphrodites and pseudo-hermaphrodites. In a further article (1945a) he summarizes his own and the highly confirmatory findings of Jensch (1941). On a much smaller material, Darke (1948) failed to find any deviation of the sex-ratio among relatives of homosexuals, but his numbers are too small to be of much value. The sex-ratio among sibs is also the main theme of an article by Slater (1944b), where evidence is produced that it is in part hereditarily determined. It also appears in some very valuable statistics collected by Julia Bell (1940): in 49,000 in-patients of general hospitals, the sex-ratio varies enormously in various pathological conditions, from an 86 per cent. male incidence in hernia to an 11 per cent. incidence in goitre. This paper also establishes that in this country one may expect to find 0.61 per cent. of persons to the offspring of first cousins, a useful standard for the detection of recessivity in pathological conditions.

In the foregoing review no attempt has been made to cover recent literature on general genetics, the genetics of mental deficiency, the incidence of mental disorder and population studies, non-genetical aspects of constitution, or eugenics.

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BIOCHEMISTRY OF THE NERVOUS SYSTEM.

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INTRODUCTION.

BIOCHEMICAL research has been taken up again with renewed vigour after the temporary set-back due to the war. Progress can be reported in many directions during the period under review, 1944-1949, and particular interest has been shown in the physiological aspects of biochemistry, which attempt to link the data derived from studies on isolated tissue preparations with the changes occurring during the activity of the organism as a whole. There has been a noticeable widening of the field as biochemistry has been applied to an ever-increasing range of problems. Applications in endocrinology have led to the stage at which a number of the endocrine principles have been isolated in the pure chemical state and the actions of some of them can be reproduced with tissue preparations in the test-tube. The old boundaries between biochemistry and endocrinology are thus becoming less easy to define as these two branches of science grow increasingly close together. The development of micro-methods during the last few decades enabled the biochemist to work with quantities of the order of a few milligrams: recent work on paper chromatography and ultraviolet microspectrophotometry has developed a series of new techniques in which it is possible to work with micrograms. The possibilities of radioactive tracer methods in this field are beginning to be explored. It has not been possible in the present review to do justice to all the investigations carried out in these many fields. The reviewer has therefore aimed at indicating where information on different topics can be obtained, rather than at attempting to give a comprehensive account of every significant piece of research.

The recent foundation of an extensive new laboratory for biochemical research in psychiatric problems at the McLean Hospital, Massachusetts, under the direction of Dr. Folch, may be mentioned as an event in this field that will be welcomed by all.

1. *Metabolism of the Brain in Vivo.*

Four main methods are available for studying the metabolism of the brain during life. These are (1) the measurement of the overall metabolism of the whole brain by analysis of the blood entering and leaving the brain; (2) direct analysis of brain tissue after rapid fixation by freezing in liquid air; (3) the study of the course taken in the brain by metabolites labelled with radioactive or other isotopes, and (4) the measurement of local changes in the oxygen tension and pH by the insertion of suitable electrodes into the brain. These methods have been supplemented by a number of more specialized techniques,

such as the use of histochemical methods for studying changes in the distribution of cell constituents. Use has also been made of the electrical rhythms in the brain as an indicator of cerebral function in studying the effects of biochemical factors such as anoxia and hypoglycaemia on the metabolism of the brain.

(a) *Metabolic activity by arterio-venous differences.*—The calculation of the metabolic activity of the brain in the normal state requires a knowledge of (a) the rate of blood flow through the brain, and of (b) arterio-venous differences in the oxygen, glucose and carbon dioxide content of the blood. Recent work has confirmed the high metabolic activity attributed to the brain by the older investigators. Kety and Schmidt (1945, 1946) measured the blood flow by determining the rate at which cerebral venous blood acquired nitrous oxide from arterial blood: they found an average rate of flow of 62 ml. blood/100 gm. tissue/min. in the brain of normal young men, which indicated that about a fifth of the blood leaving the heart flowed through the brain. The cerebral oxygen consumption was 3.7 ml. O_2 /100 gm. tissue/min.; they concluded that the brain could account for as much as a quarter of the metabolism of the whole body under basal conditions. These values of Kety and Schmidt are somewhat higher than the values 45.4 ml. blood/100 gm. tissue/min. for the blood flow and 2.9 ml. O_2 /100 gm. tissue/min., which may be calculated from the figures obtained by Gibbs, Maxwell and Gibbs (1946), who measured the rate of blood flow by injecting Evan's blue into the right internal carotid artery and estimating it in blood taken simultaneously from the left internal jugular vein and the femoral artery. In a more recent investigation Kety and Schmidt (1948) obtained the further values of 54 ml./100 gm./min. for the blood flow, and 3.3 ml. O_2 for the cerebral oxygen consumption.

While such assessments are of considerable value as approximate indications of the metabolic activity of the brain, the accuracy of the figures obtained is not beyond question. The methods depend on the assumption that blood samples taken from the internal jugular vein are representative of mixed cerebral venous blood: but it is well known that such blood may contain variable amounts of blood from the face, scalp and the bones of the skull. Ferris *et al.* (1946) and Himwich *et al.* (1947) have claimed that, owing to the asymmetry of the venous sinuses draining the cranium, the blood of the internal jugular vein may contain a different proportion of extracranial blood on the two sides. The composition of the blood showed significant differences in the left and right jugular veins in 14 out of 21 subjects who were tested, and on this fact they based a method of determining the extent of admixture of extracranial blood in any particular subject. They concluded that internal jugular venous blood obtained in man by the traditional technique cannot be considered as representative of mixed cerebral venous blood, and that, therefore, it is of limited value in the study of cerebral blood flow or metabolism in man. The same objection applies to several methods of estimating the cerebral blood flow (the plethysmographic method has also been criticized by Gregg and Shipley, 1944). While such criticism may be well founded for some previous work, it should not be taken as invalidating all the work on the metabolism of the brain: it indicates rather that a correction should be applied

in some cases and, since the metabolism of the brain is likely to be greater than that of the extracranial tissues, the correction would be expected to increase rather than to diminish the high values hitherto obtained for the brain metabolism *in vivo*.

In this connection it may be mentioned that, in view of the relative inactivity of the white matter, the metabolic activity of the grey matter in the brain must be considerably higher than the values obtained for the whole brain. We have little information as yet as to the actual rate of metabolism of localized regions of the brain; but Bronk, Larrabee and Davies (1946) have obtained figures by means of the "oxygen electrode" for the oxygen consumption in the region of the presynaptic endings and of the cell bodies. Further information on this point was obtained by Davies and Rémond (1947), who were able to demonstrate local differences in the oxygen tension in the neighbourhood of the superficial arterioles and venules of the cerebral cortex.

The older work on the metabolism of the brain showed little change in mental disease. Himwich and Fazekas (1944) found no significant difference from the normal in undifferentiated mental defectives; but they reported a reduced metabolic activity of the brain in subjects suffering from mongolism, cretinism, phenylketonuria, amaurotic familial idiocy, microcephaly and advanced hydrocephaly. In animal experiments, Fazekas (1946) found nearly normal figures for the brain metabolism in thyrotoxic, thyroid deficient and cretinous rats. Gibbs *et al.* (1947) have reported normal figures for the inter-seizure blood flow and cerebral metabolism in epileptics. In discussing the accuracy of their methods they suggest that the validity may be improved by making the jugular vein puncture high up under the mastoid, so that contamination by blood from extracerebral areas can be reduced to a minimum. A careful reinvestigation of the cerebral blood flow and oxygen consumption in 22 schizophrenics by the nitrous oxide technique gave no evidence of any deviation from normal values. There was also no measurable change associated with a significant clinical change produced by administering sodium amytal (Kety *et al.*, 1948).

In contrast to these negative findings Kety *et al.* (1948) have reported a significant fall of 40 per cent. in the cerebral oxygen consumption of comatose diabetics: the figures varied from 2.4 ml. O_2 /100 gm./min. for subjects who still retained consciousness to 2.1 or less for those in deep coma. The depression in the oxygen consumption was related to the severity of the ketosis rather than to the acidosis of the patients: in this condition, as also in insulin hypoglycaemia, the fall in the cerebral oxygen consumption is apparently responsible for the coma.

Geiger and Magnes (1947) have described a new method for the isolation of the cerebral circulation and perfusion of the brain in the living cat. They occlude all the normal venous outlets from the brain and collect the whole of the venous blood from the brain by tapping the occipital sinuses. With this preparation the oxygen consumption was again found to be related to the degree of cerebral activity: it was increased by analeptics, and decreased by narcotics.

A survey of the cerebral oxygen consumption in mammals of different sizes has shown that the metabolic activity of the brain varies much less than that of other organs throughout the series (Grande, 1950). Thus the basal metabolic rate is more than ten times higher in the mouse than in the horse, varying roughly with the 0.73 power of the weight: but the cerebral oxygen consumption shows relatively little variation. In an analogous investigation on tissue slices Elliott (1948) has concluded that the oxygen uptake of the cerebral cortex is roughly inversely proportional to the tenth root of the average body weight of the individual adult of the species. He found considerable individual variation within a species, and even in tissue slices from different parts of the cortex in the same brain. Kinetic measurements on tissue slices are less easy to evaluate than measurements on the whole animal *in vivo*, but these results agree in showing that the metabolic activity of the brain is more constant than for other tissues. It may be noted that the brain, unlike most of the other tissues, is functionally active in the normal resting state.

Folch (1947) has reported calculations of the cerebral oxygen consumption in man at different ages down to birth. In view of the relatively greater size and development of the brain in comparison with the rest of the body in the infant, he estimates that more than a half of the total oxygen consumption during the first few years of life is due to the brain, which therefore occupies a central position in the energy balance of the whole organism. The reason why the brain requires such a high expenditure of energy is still not known, but it is clear that the brain requires a continuous large inflow of energy which is increased in certain kinds of functional activity, but is also large in the normal resting state.

2. Analysis of Brain Tissue.

In any attempt to find out about the biochemical changes occurring in the brain *in vivo* the chief difficulty is that of devising a satisfactory method of obtaining specimens of brain tissue for analysis. The method must be rapid enough to avoid post-mortem glycolysis, which is very rapid in the brain: at the same time it is necessary to avoid the use of anaesthetics, which affect the metabolism, or procedures such as decapitation, which cause stimulation of the brain. The method of fixing the tissue by freezing the brain *in situ* with liquid air has now come into general use. Much of our recently acquired knowledge of the changes occurring in the brain *in vivo* depends on the use of this method.

(a) *Fixation with liquid air.*—Liquid air can be applied directly to the exposed cortex of the larger laboratory animals, such as the morphinized dog or the cat; but the method is particularly applicable to smaller animals, such as the rat and the mouse, which can be killed and, at the same time, frozen solid in a matter of seconds by immersion in liquid air. Under these conditions no anaesthetic is required.

It might be thought that the application of liquid air would cause considerable stimulation of the central nervous system; but the method gives high figures for phosphocreatine, which is rapidly broken down when the brain is stimulated and which can therefore be used as an index of the degree

of stimulation of the brain. It is also significant that the figures given by this method for the brain lactic acid are very low, which indicates that there is no serious error due to post-mortem glycolysis. Figures obtained for normal rats in the sleeping state (average 12.2 mgm. per cent. lactic acid) come close to the figure 9.8 mgm. per cent., obtained for anaesthetized animals, and here the anaesthetic would greatly reduce any excitation of the brain by the liquid air (Richter and Dawson 1948a).

These figures contrast with the relatively low phosphocreatine and high lactic acid values obtained in brain samples taken after decapitation. The difference cannot be attributed to the greater speed of fixation of the tissue with liquid air, for it takes as long as 16 seconds to freeze right through the brain of even a small animal, and it takes about 30 seconds to freeze the brain of a larger animal to a depth of 1 cm. It may be that while the wave of freezing is spreading through from the surface the circulation of the interior parts of the brain remain intact, so that post-mortem changes due to anoxia do not commence immediately the freezing of the brain is started. A more important reason for the apparent absence of stimulation is that the intense cold blocks the nervous transmission from the periphery so that the procedure is painless (Richter, 1950). This agrees with the rather surprising observation of Olsen and Klein (1947a) that, unlike strychnine and other irritants, liquid air causes relatively little stimulation of the central nervous system of the cat, when applied directly to the surface of the brain. It is known that "post-mortem glycolysis" can be reduced if the animal is anaesthetized before killing. It would appear that the rapid glycolysis which occurs within a few seconds after decapitation should be attributed to the stimulation of this procedure rather than to the post-mortem state; for glycolysis can be produced without death if the brain is stimulated, while it occurs only relatively slowly if the animal is killed by methods which avoid violent stimulation of the brain.

For the purposes of biochemical investigation, the phosphocreatine and lactic acid figures suggest that the liquid air fixation procedure is comparable to fixation under conditions of rapid anaesthesia rather than to fixation after decapitation, which involves violent stimulation of the brain. Since it limits the extent of post-mortem change, the liquid air technique represents a real advance and it has enabled new evidence to be obtained of the biochemical changes occurring in the brain *in vivo* in different physiological states.

3. *Changes Associated with Functional Activity of the Brain.*

The metabolic activity of the brain, as indicated by the utilization of glucose and oxygen, is reduced during narcosis and increased during convulsions. Direct determination of the metabolites in the brain by the liquid air technique has shown that there is a considerable breakdown of phosphocreatine when the brain is stimulated by convulsant drugs or by electric shock treatment. Stimulation also produces a liberation of lactic acid and of inorganic phosphate in the brain.

The evidence at present available indicates that the energy supplied by the combustion or glycolysis of glucose is first converted into "high-energy" phosphate bonds by coupled phosphorylation reactions. These are then

available to give energy for the synthesis of acetylcholine or for other processes connected with the electrical changes and functional activity of the brain. Our knowledge of these processes is still very inadequate, but the following scheme illustrates one of the possible pathways by which the energy may be handed on through a series of coupled reactions and so utilized for the functional activity of the cell.

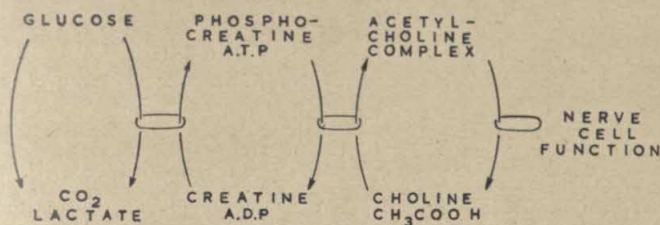


FIG. 1.

Experiments *in vitro* have indicated that phosphocreatine is in dynamic equilibrium with adenosine triphosphate (ATP), and these high-energy phosphate esters represent an energy reservoir which is available for synthetic processes of many kinds. The energy derived from the oxidation of one molecule of glucose can build up 38 molecules of ATP. Energy for the synthesis of "high-energy" phosphate bonds can also be derived from the glycolytic breakdown of glucose to form lactate. The energy liberated by the breakdown of phosphocreatine or ATP can be used for the synthesis of acetylcholine and for other processes concerned in the functional activity of the brain.

(a) *Anoxia*.—The brain is specially sensitive to anoxia, which affects the circulation as well as the overall respiratory exchange (Noell, 1944). Gurdjian, Stone and Webster (1944) have studied the effect on the dog brain of gradually reducing the oxygen tension. At tensions which brought the saturation of the venous blood from the brain below 28–43 per cent., there were changes in the EEG pattern and an increase in the lactic acid content of the brain; but the phosphocreatine and ATP levels were not much affected until the oxygen saturation had been further reduced to 15–22 per cent. Since the change in the electrical rhythms occurred long before there was any considerable fall in the phosphocreatine or ATP content, they concluded that oxygen must play a more active part in relation to the electrical activity of the brain than that of merely effecting the oxidative resynthesis of high-energy phosphate esters. A similar conclusion was drawn from the observation that anoxia inhibits the convulsive activity induced by metrazol or by insulin hypoglycaemia (Gurdjian, Webster and Stone, 1947).

The effects of cyanide poisoning run closely parallel to those produced by anoxia. Albaum, Tepperman and Bodansky (1946) found a decrease in the phosphocreatine, ATP and glycogen of the brain, and an increase in lactate, inorganic phosphate, phosphoglycerate and phosphopyruvate when sodium cyanide was administered to the rat. Similar findings have been reported in cyanide poisoning in the cat. As in anoxia, changes in the electrical activity of the brain were seen before the high-energy phosphate esters were extensively

broken down: the rate of glucose utilization was increased, but the anaerobic processes were not sufficient to maintain the functional activity of the brain (Olsen and Klein, 1947a).

Impairment of visual discrimination is often an early sign of cortical dysfunction in anoxia. Proger and Dekaneas (1946) were able to show that impairment of vision and reduced performance in decoding tests could be correlated with changes in the EEG.

(b) *Convulsions*.—The changes in the metabolites of the brain in convulsive activity are similar in many respects to those in anoxia: the changes are those associated with increased breakdown of high-energy phosphate esters and increased utilization of glucose and oxygen.

Convulsions are frequently accompanied by anoxemia, due to impairment of the respiratory function, and the observed changes might therefore be ascribed to the incidental lowering of the oxygen tension in the blood. For this reason, Stone, Webster and Gurdjian (1945) studied the changes in the dog brain in convulsions under conditions in which anoxemia was eliminated by the use of artificial respiration and immobilization of the musculature with dihydro- β -erythroidine. Simultaneous records were made of the EEG and the oxygen saturation of the blood. Their experiments established that the biochemical changes associated with convulsions still occurred when the oxygen saturation of the cerebral blood supply was maintained at a high level: the changes could not therefore be attributed to the lowering of the oxygen tension of the arterial blood.

Recent measurements of the circulatory changes after the administration of convulsant drugs have given little support to the old idea that the convulsions could be attributed to cerebral anoxia caused by spasm of the cerebral blood vessels. Generally no preconvulsive diminution in the cerebral circulation is observed, but there is a considerable increase during and after the convulsions (Davis, McCulloch and Roseman, 1944). A similar increase in the cerebral circulation has also been observed after electrical stimulation of the brain and during epileptic seizures (Darrow, 1949). This may result from the vasodilator action of the CO_2 , formed as a result of increased metabolic activity, or it might be mediated by the action of acetylcholine on the cerebral blood vessels.

The increased activity of the brain during convulsions was shown by the increased oxygen consumption of the brain of the monkey in convulsions (Schmidt, Kety and Pennes, 1945). This agrees with the previous observations with the "oxygen electrode," which showed a marked fall in the oxygen tension of the brain tissue before the commencement of convulsions (Davis, McCulloch and Roseman, 1944). Davis and Rémond (1947) have followed up this line of investigation with direct measurements of the oxygen consumption of the cortex *in vivo*, using an elegant method in which they perfuse a small isolated area of the cortex. These experiments again showed an increased oxygen consumption during status epilepticus induced by metrazol injection in the cat: but the investigators did not find that the increased oxygen uptake preceded the increased electrical activity of the cortex. Richter and Dawson (1948b) and Dawson and Richter (1950) have studied the changes in the brain

after electrical stimulation, with particular attention to the time relations of the changes. They found the breakdown of phosphocreatine was remarkably rapid: as much as 50 per cent. of the total brain phosphocreatine was lost in specimens fixed in liquid air after 1 sec. of electrical stimulation. At the same time there was a corresponding rise in the calcium-soluble "hexose phosphate" fraction, indicating an immediate transfer of phosphate from phosphocreatine to glucose or glycogen. During the first few seconds of stimulation there was also a liberation of ammonia and a rapid fall in the acetylcholine content of the brain (Richter and Crossland, 1949). There was only a very slight fall in the level of ATP. It is noteworthy that these changes occurred several seconds before the onset of convulsions, which may not start for 10 sec. or more after the electrical stimulation. These primary metabolic changes were an immediate result of the electrical stimulation and not of the convulsions.

The primary changes were followed by the return of the hexose phosphate fraction to the normal level with a liberation of inorganic phosphate, in brains fixed up to 10 sec. after the cessation of electrical stimulation. At the same time there was a complete resynthesis of acetylcholine.

During the period from 15-50 sec. after electrical stimulation, while intermittent convulsions were in progress, the acetylcholine level again fell, but the phosphocreatine, ATP and inorganic phosphate all returned gradually to their normal levels. This period corresponds to the period of increased circulation and increased utilization of oxygen and glucose by the brain. It appeared that the acetylcholine was the most labile metabolite under these conditions, and it reflected most closely the functional state of the cortex.

These observations are in general agreement with those of Klein and Olsen (1947b) who studied the effects of convulsant drugs and electrical stimulation on the metabolites of the cat brain. They found a significant *fall* in convulsions in the brain glucose, glycogen, phosphocreatine and ATP, with a *rise* in lactic acid, ADP and inorganic phosphate. They found no significant change in the pyruvate, creatine, creatinine or hexose phosphate fractions, but the conditions of their experiments were such that they could not have easily detected the transient changes in the hexose phosphate fraction observed by Dawson and Richter (1950).

Cicardo (1945, 1946) observed an increase in the acid-soluble phosphorus of blood withdrawn from the superior longitudinal sinus after stimulation with picrotoxin or metrazol in the dog. This rise was specific for blood coming from the brain, for it was not observed in blood from the femoral vein or artery: it continued for about 15 min. after stimulation. Using the same method, a loss of potassium from the dog brain was observed during electrically induced convulsions. Colfer (1947) found no significant loss of potassium from the brain as a whole during convulsions, but he reported a change in the distribution of potassium: using the microincineration technique he found an apparent shift in the potassium from the neurons to the extracellular spaces of the tissue. At the same time there was an increase in the neuronal sodium. These changes, which were observed consistently in the rat, rabbit, guinea pig, dog and monkey,

are in agreement with the ionic changes reported by Hodgkin and Huxley (1947) on stimulation of the isolated giant axon of the squid.

Spiegel-Adolf *et al.* (1945) have reported the appearance in the CSF, after electro-shock treatment, of a substance which may be a purine or pyrimidine derivative, as it gives an ultra-violet absorption band at 2,550–2,950 Å. Richter, Dawson and Rees (1949), reinvestigating an older report that ammonia is liberated into the CSF in epileptic convulsions, were unable to find any significant amount of ammonia in the CSF, after epileptic or electrically induced convulsions in man.

The source of ammonia liberated in the brain on stimulation is not yet clear, but in anoxia or in electro-shock treatment the level may rise to as much as 1 mgm. per cent. NH_3 before the onset of convulsions; it has therefore been suggested that the toxic action of the ammonia, which is a powerful cerebral stimulant, may play a part in the initiation and spread of the cerebral discharge (Richter and Dawson, 1948*b*). Another factor is likely to be the acetylcholine level, which was observed to rise to a relatively high level before the convulsions started. Forster (1945) has shown that acetylcholine can produce cortical activity resembling that in epileptic seizures. The role of acetylcholine in relation to convulsive activity has been recently discussed by Pope *et al.* (1947) and by Hyde, Beckett and Gellhorn (1949). It may be expected that each of these factors is closely connected with the precipitation and spread of the cortical discharge.

(c) *Head injury and shock.*—There are special difficulties in interpreting the changes which occur in the brain in trauma and shock. There may be general anoxemia due to respiratory failure and anaemia due to circulatory collapse. Cerebral oedema, localized or general, may again cause localized ischaemia through interference with the normal venous drainage of the brain. Such factors are difficult to control and may vary from one experiment to another, making it hard to obtain consistent results.

Blalock (1944) reported that the metabolism of the brain was increased, as indicated by an increased oxygen uptake even before the blood pressure began to fall, in traumatic shock; but Gurdjian, Webster and Stone (1944) found surprisingly little change in the circulation and metabolism of the brain in morphinized dogs which had been subjected to severe head injuries. Areas of the cortex showing no macroscopic evidence of damage generally showed little change in the tissue metabolites, but areas of contusion gave greatly increased lactic acid and inorganic phosphate, with decreased phosphocreatine and ATP values. The changes were similar to those in anoxia.

The publications of Le Page (1946*a* and *b*) on the biochemical changes in the tissues in shock have received a good deal of comment. The methods of producing shock included (a) "tumbling" in a rapidly revolving drum, (b) ischaemia of leg muscles, (c) poisoning with nembutal, and (d) haemorrhage. A point of some interest was his observation that tumbling in the drum produced relatively little shock in rats previously conditioned to the treatment, while in normal animals it could produce death in 15 minutes. His attempt to carry out parallel estimations of no less than 15 tissue metabolites in the rat brain is commendable; but the reported values show large individual variation and

they differ, to some extent, from those observed by other workers. He reports the presence of considerable amounts of free adenylic acid in the brains of normal animals, although the phosphocreatine level was high: his figures for pentose phosphate and phosphoglyceric acid are also surprising. The biochemical methods he used have been criticized (Gurdjian, Webster and Stone, 1947).

Spiegel *et al.* (1947) have shown that cerebral concussion inhibits metrazol convulsions in the rat and the cat. They found no significant differences between normal and concussed animals in the respiratory rate of excised brain slices. Measurements of the polarizability of the brain suggested a transitory period of impairment of the cellular membranes after concussion. They also observed the presence of an active nuclease in the CSF of patients and experimental animals following cerebral concussion: at the same time, the CSF contained a substance absorbing at 2,650 Å. in the ultra-violet range. They suggest that this may be a nucleic acid degeneration product associated with the process of chromatolysis.

Bornstein (1946) found that appreciable amounts of acetylcholine appear in the CSF after a blow on the head. She suggests that the functional state of the cells of the brain is affected by acetylcholine issuing from injured cells into the extracellular spaces. In agreement with this she was able to show that atropine, which blocks some of the effects of acetylcholine on the brain, abolishes the characteristic EEG changes following a blow and counteracts the stupor.

It is noteworthy that although the changes in the brain in head injury are qualitatively similar to those occurring post mortem, they are not quantitatively identical. Gurdjian, Webster and Stone (1944) observed that in spite of the high lactic acid and low phosphocreatine level in areas of contusion, the ADP and adenylic acid levels were relatively much lower than are found post mortem. Le Page (1946a) also noted that methods of cerebral stimulation gave relatively high brain lactic acid levels: the brain lactic acid figures for animals in shock were 20–75 per cent. higher than those of animals which had been killed and incubated for 20 min. post mortem.

(d) *Anaesthesia*.—It might be expected that the changes in the brain in anaesthesia would be the reverse of those associated with cerebral stimulation, and the experimental results have generally supported this expectation. Studies of arterio-venous differences have shown a reduction of cerebral metabolism in the brain during anaesthesia. Determinations of the tissue metabolites by the liquid-air fixation method have indicated a building up of the high-energy phosphate esters, while there is a fall in the lactic acid and inorganic phosphate. Olsen and Klein (1947b) failed to find any differences from control animals in anaesthetized cats previously treated with dihydro- β -erythroidine and maintained in artificial respiration; in this work the brains were frozen by pouring liquid air on the previously exposed skull. But Stone (1948), Le Page (1946a), and Richter and Dawson (1948a) have all observed changes in the brain in anaesthesia, with the more rapid freezing which is possible in working with smaller animals.

Richter and Crossland (1949) have confirmed with the liquid-air technique a previous report of Tobias, Lipton and Lepinat (1946) that the acetylcholine

content of the brain is raised in anaesthesia: the mean acetylcholine content for anaesthetized rats was 50 per cent. higher than that of normal controls. If, as has been suggested, convulsive phenomena depend on the acetylcholine level, this might help to explain some of the excitatory effects of anaesthetics and, in particular, the action of barbiturates in increasing the incidence of larval attacks and seizure patterns revealed in epileptics by the EEG.

The brain ammonia level, which appears to be related to cerebral irritability, shows little immediate change in anaesthesia; but it falls to a very low level in deep nembutal anaesthesia lasting for half an hour or more (Richter and Dawson, 1948b). Experiments with the radioactive isotope of phosphorus have indicated that there is some inhibition of the synthesis of radioactive nucleoproteins and phospholipids during prolonged nembutal anaesthesia in the mouse (Dawson and Richter, 1949). Harrevel (1947) has shown that anaesthetics depress the asphyxiation-depolarization potential led off from the cerebral cortex in the cat. On this and other evidence he has based a new theory of narcosis.

From a series of experiments on 15 rabbits and 50 mice it was concluded that ether anaesthesia causes a significant rise in the brain glycogen content: the rise in the rabbit was from 130 to 223 mgm. per cent., and in the mouse from 160 to 201 mgm. per cent. (Ivanenko and Voinar, 1942). An increase in glycogen in anaesthesia agrees with the reduced utilization of carbohydrate, but it would appear that care is needed in interpreting these observations, for Chance and Yaxley (1949) have found an increase in glycogen in the brain after convulsions in the mouse. Hevesy (1949) has shown that urethane narcosis causes an increased uptake of acetate labelled with radioactive carbon into the carbon compounds of the brain and other tissues: this is attributed to the reduced metabolic activity, which limits the dilution of the isotope. Velasquez and Membrado (1944) have reported that anaesthesia reduces the acetylcholine content of CSF withdrawn by cisternal puncture from the dog.

(e) *Emotional excitement and sleep*.—Richter and Dawson (1948a) have carried out a series of experiments by the liquid-air fixation method to test whether biochemical changes could be detected in the brain with changes of functional activity under normal physiological conditions. The brains of rats taken in the sleeping state gave a significantly lower lactic acid content than controls in the normal waking state; rats taken during emotional excitement (produced by withdrawal of support) gave a brain lactic acid level considerably higher than the normal, and over 300 per cent. above the mean level for sleeping animals. It could be shown that the rise in emotional excitement was not due to concomitant muscular activity, since (a) it still occurred after immobilization of the muscles with tubocurarine, and (b) no rise in the brain lactic acid was produced by vigorous muscular exercise alone. The rise in the lactic acid in the brain in emotional excitement was a relatively rapid process: it was reversible and the lactic acid returned to normal within a few minutes when the excitation was discontinued.

Determinations of the brain acetylcholine content have shown that here again there are changes associated with functional activity of the brain. The acetylcholine level is significantly higher than normal during sleep, and the

level is decreased during emotional excitement (Richter and Crossland, 1949).

It is noteworthy that the changes in the brain in emotional excitement differ qualitatively and quantitatively from those occurring in convulsions or in post-mortem autolysis. In each of these conditions there is a liberation of lactic acid, but there is no significant liberation of ammonia or accumulation of inorganic phosphate in emotional excitement and, instead of a fall, there is a significant rise of as much as 13 per cent. in the phosphocreatine level (Dawson and Richter, 1950). This suggests that, in spite of the increased metabolic activity of the brain indicated by the fall in acetylcholine and the liberation of lactic acid, the improved supply of glucose and oxygen to the brain in emotional excitement is sufficient to maintain the high-energy phosphate esters at a high level.

In a series of studies on the phosphorus metabolism of the brain *in vivo* by the method of administering radioactive P^{32} as a tracer, Borell and Örstrom (1947) found that the pineal gland has the highest turnover of phosphorus of any part of the brain. The metabolically active phosphate esters are mainly responsible for the phosphorus exchange. Next to the pineal gland in phosphorus turnover came the anterior and posterior lobes of the hypophysis and then the choroid plexus. The P^{32} turnover is greater in the adenohypophysis than in the tuber cinereum, but the turnover is increased in both in pro-oestrus, indicating that they operate together as a functional unit. Extirpation of the eyes caused an increase in the P^{32} turnover of the medulla oblongata (Borell, Westman and Örstrom, 1948). The high activity of the pineal gland has been confirmed by Reiss, Badrick and Halkerston (1949), who showed that it also gives a high turnover of radioactive iodine. The phosphorus turnover of the rat brain was increased after hypophysectomy, but it could be restored to normal by treatment with adrenocorticotrophic hormone. Borell *et al.* (1947) found no difference between oestrus and anoestrus in the P^{32} turnover of the tuber cinereum, adenohypophysis or ovaries of the female rabbit, but castration produced an increased turnover in the adenohypophysis. There was also a localized increase in the P^{32} turnover of the hypophyseal system accompanying coitus in the rabbit.

The biochemical changes in emotional excitement are not limited to the relatively labile metabolites such as the phosphate esters, but they also extend to the more stable structural elements of the cell. Experiments with P^{32} as a tracer element have shown that a period of prolonged excitement, induced by leaving for 3 hours in a slowly rotating drum, produces a significant fall of 25 per cent. in the rate of synthesis of radioactive phospholipid in the brain of the mouse (Dawson and Richter, 1949). Here again it could be shown that the effect was not attributable to concomitant muscular exercise, since it was absent in animals previously conditioned to running in the drum. The evidence suggests that there is an interference with the normal metabolism of the structural elements of the cell in emotional excitement, when the biochemical mechanisms of the cell are being used for functional activity of another kind. Hevesy (1949) has recently reported that the rate of incorporation of acetate labelled with radioactive carbon into the carbon compounds of the brain was

reduced by a period of exercise in which a series of mice were made to swim for 20 min. Here the change is attributable to an increased activity of the labile metabolites, leading to a more rapid dilution of the radioactive carbon.

(f) *Brain metabolism and electrical activity.*—One of the chief difficulties in the experimental study of brain metabolism has been the lack of a satisfactory means of recording cerebral function. With other organs, such as the liver or kidney, the functional activity can be stated, to some extent, in biochemical terms, but this is clearly impossible for the brain. The recent use of the EEG. as an indicator of cerebral function, represents a considerable advance, especially as this can be used in animal experiments as well as on human subjects. The EEG. changes produced by biochemical factors, such as anoxia and hypoglycaemia, show a close agreement with the changes in the mental state: they can therefore be used in experimental investigations as an indicator of cerebral function. Various aspects of this approach have been discussed by Darrow (1947) and by Hill (1950), and as they are reviewed elsewhere in this volume only a few relevant points will be mentioned here.

That the electrical rhythms of the brain should be sensitive to changes in the biochemical milieu is not surprising in view of the ionic or chemical origin of the electrical potentials of all animal tissues. Nerve cells, like muscle and gland cells, clearly produce electrical potentials as a result of the chemical reactions occurring during their normal metabolism. The phenomena of oscillation and repetitive discharge in simple systems have been investigated by Bronk (1949), who has pointed out their relevance to the study of the electrical rhythms of the brain. From an analysis of the factors determining the frequency of rhythmic discharges in the isolated stellate ganglion of the cat, he concludes that the recurring impulses arise from a "local oscillatory state" which is characteristic for each type of cell or axon. Repetitive discharge frequencies of the order of 5–10 c./sec. were obtained with this preparation, and the frequency could be varied by changing the concentrations of calcium, potassium and acetylcholine ions in the surrounding medium. Hodgkin (1948) has studied the conditions for repetitive discharge in isolated axons of the crab, with which he obtained discharge frequencies varying from 5 to 150 c./sec. Numerous observations on the effects of different ions on the frequency of oscillatory discharge of neurons have been recorded by Lorento de Nô (1947). It may be noted that rhythmic changes of this kind are not restricted to the tissues of living organisms: rhythmic or periodic reactions have long been known to occur in purely chemical systems and the dynamics of such chemical oscillators have been worked out (Hedges and Meyers, 1926).

Kaufman and Hoagland (1946) have regarded the electrical rhythms of the brain as depending on the activity of a system of chemical pacemakers. A series of different experimental approaches have agreed in showing that alpha activity is slowed by factors which reduce the rate of cerebral respiration and accelerated by factors which increase it: they conclude that in changes of alpha frequency occurring over not too large a range, the change is probably proportional to the change in velocity of a chemical pacemaker involved in a series of enzymatic reactions linked with cerebral respiration. Changes in alpha frequency with temperature followed the Arrhenius equation. Brazier

and Finesinger (1945) have also interpreted EEG frequency changes as attributable to changes in metabolic activity. Acceptance of the essentially electrochemical nature of the electrical activity of the brain presents no difficulty except to the few who would attempt to dissociate the electrical and chemical aspects, regarding the electrical as more important and relegating the chemical to a subordinate role, such as that of the chemicals in a Leclanché cell (Walter and Walter, 1949). That would ignore a great deal of evidence, and in particular the evidence of the sensitivity of the cerebral rhythms to small changes in the ionic milieu and metabolic activity of the brain. It would appear more reasonable to regard both the electrical and the chemical phenomena as essential components of a combined electrochemical process.

The changes in the EEG in anoxia correlate well with the onset of failure in mental efficiency, as indicated by handwriting and other tests, and this is a matter of some practical importance in connection with the study of high-altitude flying. Trains of slow waves at 5-7 c./sec. are observed when the oxygen saturation in the internal jugular vein falls to 30 per cent. The biochemical factor immediately concerned in this initial change is still unknown. Gibbs *et al.* (1943) maintained that the EEG changes in hypoxia, produced by breathing 6-8 per cent. O_2 , are related primarily to the decrease in CO_2 tension which occurs. However, Gurdjian, Webster and Stone (1949) found in experiments on the morphinized dog that the CO_2 tension played very little part in regulating the ECoG, either in the presence or in the absence of an adequate supply of oxygen: the CO_2 tension could be varied through a large range without producing much effect. It appeared possible that the reduced oxygen tension might act indirectly by lowering the concentration of high-energy phosphate esters: but determinations of the tissue metabolites after freezing the brain with liquid air showed that the EEG changes occurred before there was any significant change in the brain lactic acid, glucose, glycogen, inorganic phosphate, phosphocreatine or ATP. This suggests that oxygen influences the EEG through some mechanism other than the carbohydrate and phosphorus metabolism.

Gellhorn and Hymans (1948) have found that convulsive potentials produced by the local application of convulsant drugs to the cerebral cortex of cats and dogs, are much more sensitive to anoxia than the normal activity of the cortex. Convulsive potentials are abolished by anoxia or asphyxia at a time when the normal potentials are practically unchanged. On readmission of oxygen the normal potentials appear before the convulsive spikes reappear: there is then a period of "rebound" in which the frequency of spikes is greatly increased.

4. Nervous Conduction and Transmission.

Considerable advances in our knowledge of conduction in the nerve axon have been made during the period under review. Until recently it was generally believed that the nerve action potential arose from a transient breakdown of the polarized layers of the plasma membrane, but there has been a growing dissatisfaction among investigators in this field with the mechanisms that have been put forward to account for the existence of the membrane potential, and the changes occurring during the passage of a nervous impulse. The interior

of a nerve axon is negatively charged with respect to the exterior, and, on the classical view, the action potential produced by the breakdown of the insulating membrane would be expected to be slightly less than the resting nerve potential. Hodgkin and Huxley (1945) have measured the resting and action potentials of the giant axon of the squid, using a fine silver micro-electrode inserted down the middle of the fibre. They found that the action potential is in fact nearly double the resting potential. Conduction of a nervous impulse thus involves not merely the short-circuit of the resting potential, but an actual reversal of the resting potential, in which the interior of the axon becomes positively charged. These recent observations on the squid axon confirm a number of earlier results on crustacean nerves, and they agree with similar experiments carried out by Curtis and Cole (1942). In view of this new evidence the membrane potential theory of nervous conduction would appear to be no longer tenable in its classical form.

(a) *Kation exchange*.—Various alternative hypotheses have been suggested to account for the reversal of the resting potential in the passage of a nervous impulse, but it cannot be said that any of them has yet found general acceptance. Of particular interest is the "sodium hypothesis" of Hodgkin and Katz (1949), who suggest that conduction may involve a change in the selective permeability of the membrane to sodium ions. The resting membrane is taken to be more permeable to potassium than to sodium (so accounting for the resting potential) while the active membrane is more permeable to sodium than to potassium. A reversal of potential can thus arise, since the sodium concentration in the external medium is higher than in the axoplasm of the nerve fibre. In support of this hypothesis they have shown that the action potential of the isolated squid axon is reduced by reducing the external sodium concentration, and increased by increasing the sodium concentration in the external medium. By suitable adjustment of the ionic milieu the electrical potentials can be reduced to a small fraction of their normal values without preventing the passage of a nervous impulse. It may be noted that these experimental results emphasize the essentially electrochemical character of the electrical potentials associated with nervous activity.

Stimulation of peripheral nerve causes a liberation of potassium into the surrounding medium. This has been confirmed in some very elegant experiments of Keynes (1948), who mounted crab nerves which had previously been soaked in Ringer solution containing radioactive potassium, in a chamber over a Geiger counter tube. The rate of loss of potassium from the nerve could thus be measured directly by the loss in radioactivity, and the experiments showed a greatly increased loss of potassium on stimulation. The entry of radioactive potassium into the nerve was also increased to a smaller extent on stimulation; but as the rate of entry increased by 30 per cent. while the rate of loss increased by 300 per cent., there was a net loss of potassium from the nerve fibre. Euler *et al.* (1946) showed, with radioactive tracers administered to the cat, that stimulation of the sciatic nerve causes a 50 per cent. increase in the rate of entry of sodium, potassium and other ions. It would appear that stimulation produces an unspecific increase in the permeability, but, as Eccles (1948) has pointed out, the observed uptake of radioactive sodium and

other ions may have been entirely into the extra-axonal adipose tissue of the sciatic nerve, and not into the myelinated nerve axons. Hodgkin and Huxley (1947) have measured the extent of the potassium leakage during the passage of a single impulse in the crab nerve: they find that 1.7×10^{-12} moles of potassium leak through 1 sq. cm. of the membrane in one impulse. This is about twice the calculated amount needed to discharge the membrane capacity as required by the membrane theory of conduction.

The recovery of a nerve after stimulation must involve a process of resorption of potassium through the cell membrane. The nature of this process is not yet clear, but Krebs and Eggleston (1949) have found that the addition of *l*-glutamic acid reduces the rate of loss of potassium from brain slices suspended in saline. The building up of a high concentration of potassium in the neurons must require energy, and oxygen and an oxidizable substrate such as glucose are necessary. Shanes (1948) considers that the metabolic activity of the neuron maintains the potassium level by providing hydrogen ions which exchange with extracellular potassium ions: in support of this he was able to show that the restoring effect of CO_2 on the injury potential of frog nerve is prevented by the sulphonamides, which inhibit carbonic anhydrase. Boyle and Conway (1941) pointed out that potassium ions could be taken into the nerve cells with phosphate ions, which are then retained in the form of less diffusible phosphate esters in the cell. Support for this view has recently been obtained by Grande and Richter (1950), who studied the effect of stimulation on the exchange of radioactive phosphorus in the frog sciatic nerve. They found that the slow loss of phosphorus from the frog sciatic nerve suspended in Ringer solution is not appreciably affected by electrical stimulation; but the rate of entry of phosphate ions labelled with P^{32} from the surrounding medium is greatly increased as a result of stimulation, so that the P^{32} is concentrated in the nerve. The effect depends on the metabolic activity of the tissue and is inhibited by hydrogen cyanide.

The significance of acetylcholine ions in conduction in a nerve axon is still a matter for debate. Acetylcholine ions are surface-active and capable of depolarizing a charged membrane (Beutner and Barnes, 1948). It is believed by Nachmansohn (1946) and his associates that acetylcholine is intimately concerned in the propagation of an impulse along the axons of nerves of all kinds. The precise mechanism postulated has undergone changes, but the present hypothesis would appear to be that the acetylcholine acts by increasing the permeability of the cell membrane, which permits a local flow of current: the current liberates more acetylcholine in the adjacent regions, and so the process proceeds along the nerve axon. No satisfactory evidence in support of this mechanism has yet been advanced. The hypothesis leaves the source of the local current unexplained, and, since the acetylcholine content of sensory nerves is extremely low, this view has not found general acceptance (Dale, 1948).

(b) *Physical factors*.—It has been suggested from time to time that the nodes of Ranvier might be of significance in relation to conduction in myelinated nerve fibres. The recent development of a technique for isolating single nerve fibres from amphibian nerves has enabled the electrical and ionic exchanges at the nodes of Ranvier to be investigated (Tasaki and Mizuguchi, 1948;

Huxley and Stämpfli, 1949). Measurements of the minute electrical currents flowing in the surrounding medium during the passage of an impulse in single nerve fibres of the frog have shown that the conduction time of the longitudinal action current increases stepwise at each node of Ranvier. Conduction in the single fibres can be blocked by preventing the current from flowing in the outside medium from one node to the next: this was achieved by threading the fibres through a fine hole in a thin sheet of insulating material. Huxley and Stämpfli conclude that the process giving rise to the action current takes place at the nodes: the action potential at each node excites the next node by current flowing forward in the axis cylinder, and back in the exterior medium outside the myelin sheath. The impulse thus travels forward in a succession of little jumps, from one node to the next. This idea of "saltatory" conduction in myelinated fibres was originally suggested many years ago by Lillie, but it has not previously received much serious attention. The recent work of Huxley and Stämpfli has provided evidence in favour of the saltatory theory which appears convincing. The function of the myelin sheath is readily explained on this view: as it is an insulator it makes the local currents act a considerable distance ahead of the active region, and so greatly increases the conduction velocity of the nerve fibre. It may be noted that, contrary to certain statements in the literature, nodes of Ranvier are present in the myelinated fibres of the central nervous system as well as in peripheral nerves. (Allison and Feindel, 1949; Hess and Young, 1949.) The nodes observed in the central nervous system show the same relation of internodal length to fibre diameter as in other nervous structures. If the nodes of Ranvier have the functional significance now assigned to them they would appear to offer new possibilities for achieving variation in the mutual interaction of the neuronal circuits in the brain.

Changes in the physical state of nerves as a result of stimulation were found by Hill and Keynes (1949), who observed a measurable change in the optical opacity of the crab nerve. This occurs as an after-effect of a rapid succession of stimuli such as 250 impulses in 5 sec. Lüthy (1948) found a relatively slow change in the ultra-violet absorption bands after repetitive stimulation for 5-10 sec. Smitten (1946) has reported a number of experiments which suggest changes in the viscosity of the cytoplasm produced by stimulation in the nerve cells of the sympathetic ganglia of the frog heart: he reports that stimulation by a variety of methods results in a marked increase in viscosity. Flaig (1947) reports an apparent increase in the turgor of giant squid axons on stimulation: he concludes from his experiments that reversible 'gelation-solution' of the axoplasm may be fundamentally connected with the action current.

Biochemical factors operating *in vivo* are capable of producing very considerable changes in the electrical properties of peripheral nerves: Kugelberg (1944) found large changes in the irritability of peripheral nerves were produced by inducing states of acidosis and alkalosis in human subjects. Similar observations have been made more recently by Beyne *et al.* (1947).

(c) *Synaptic transmission*.—The liberation of cations would appear to be an essential part of the process of conduction of an impulse in a nerve fibre. Cations, which have hitherto been recognized as being liberated when nerves

of different kinds are stimulated, include potassium, acetylcholine, ammonium, thiamin, histamine and nor-adrenaline ions. By the elaboration of various ions with specific actions, vertebrate neurons seem to have utilized the general process of kation liberation to achieve specific effects in transmission at the synaptic and neuromuscular junctions. A good deal of recent work has been concerned with the elucidation of the precise roles of these various specific ions in transmission at the different effector organs throughout the body. It is now generally accepted that neuromuscular transmission from the autonomic nervous system is effected by the liberation of acetylcholine from cholinergic nerve fibres, and of nor-adrenaline, as well as adrenaline from adrenergic fibres. The recognition that the sympathomimetic substance liberated by adrenergic fibres is mainly nor-adrenaline (Euler, 1946; Gaddum and Goodwin, 1947), and not pure adrenaline, as was previously supposed, should help to clear up a number of minor difficulties in the theory of chemical transmission.

In neuromuscular transmission to the voluntary muscles the role of acetylcholine as a specific transmitter substance is now very widely recognised. Eccles (1948) explains the double phase of decay of the endplate potential by an extension of the hypothesis of the spreading surface action of acetylcholine. The temperature coefficient of the rate of decay is approximately that of a chemical diffusion process, and the actions of acetylcholine esterase inhibitors agree with the supposition that the transmitter substance is acetylcholine. It is still possible that potassium may also play a part in neuromuscular transmission (Altamirano and Huidobro, 1948; Walker and Laporte, 1947). These two ions are similar though not identical in their actions, and potassium ions can potentiate the action of acetylcholine, but the effects of potassium ions are more prolonged. Potassium ions can also act by causing a liberation of acetylcholine from the nerve terminals. It is reported by Hajdu and McDowall (1949) that the addition of 0.08 per cent. potassium ions to the Krebs solution used for suspending a strip of muscle from the denervated rat diaphragm makes it completely unresponsive to electrical stimulation, while it shows a normal response to acetylcholine. Under these conditions the muscle contracts normally, but the action potential is negligible. Here there is an apparent dissociation of the electrical disturbance of the muscle membrane and the activation of the contractile substance. It may be noted that different types of muscle show different kinds of response to acetylcholine, and the response may vary with the physiological state. Thus the rapid twitches produced by acetylcholine in mammalian voluntary muscles are quite distinct from the relatively slow, prolonged contraction in avian and amphibian muscles such as, for example, the frog rectus. It is therefore hardly to be expected that any one simple mechanism will give a universal explanation for all types of neuromuscular transmission. Von Muralt (1946) has reported the liberation of thiamin from motor nerves on stimulation, and he suggests that this may also be concerned in certain types of neuromuscular transmission.

The part played by specific ions in synaptic transmission in the brain and spinal cord is being actively investigated. Some evidence has been adduced in support of the view that synaptic transmission may be mediated by acetyl-

choline, but the evidence is still far from conclusive. It is clear that parts of the brain are highly sensitive to acetylcholine. Thus, Miller (1947) was able to show that acetylcholine in concentrations down to 10^{-7} causes a contraction of the tongue muscles of the cat when applied directly to the eserinated hypoglossal nucleus. It has similarly been reported by Artemev and Babskii (1948) that acetylcholine concentrations down to 10^{-8} increase the electrical activity of the frog brain after previous treatment with eserine. Both these effects are abolished by atropine. Again, Hyde, Beckett and Gellhorn (1949) have found that convulsive activity can be restarted after it has come to an end by the application of low concentrations of acetylcholine to the cerebral cortex.

Pharmacological evidence on the action of the anti-choline esterase drugs has been cited by Nachmansohn (1946) in support of the mediation of central transmission by acetylcholine; but Eccles (1947) concludes that the actions of acetylcholine and of the anti-choline esterases are inconsistent with the view that acetylcholine mediates synaptic transmission in the spinal cord of the frog. The observations of Richter and Crossland (1949), on rapid changes in the acetylcholine content of the rat brain during stimulation, give evidence that functional activity of the brain is associated with the breakdown of acetylcholine; the high concentrations of choline acetylase and acetylcholine esterase in the brain also give evidence that acetylcholine has some function. Dale (1948) has emphasized the point that chemical mediators, other than acetylcholine, may well be concerned in the highly specialized processes of the brain: in this connection it is of interest that Nachmansohn (1949) has recently reported the formation by choline-acetylase preparations from nervous tissues of a substance with some of the actions of acetylcholine, but apparently not identical with acetylcholine, since it could not be estimated by the chemical method of Hestrin (1949).

A great many papers have appeared in the last few years on the subject of nervous conduction and transmission. Only a few of these have been selected for mention here, but further information is available in the reviews by Feldberg (1945), Eccles (1948), Whitteridge (1948), van Harreveld and Wheldon (1948), and Lloyd and McIntyre (1949).

5. *Nerve Cell Function.*

A new approach to the study of the nervous system has been opened up by the development of the quartz-lensed micro-spectrophotometer, which combines a microscope with a photometer suitable for use with ultra-violet light. This instrument is now in use in Dr. Caspersson's Laboratory at Stockholm. By means of a photoelectric measuring device an approximate estimate can be made of the amounts of certain chemical substances within a single nerve cell. The method is applicable to substances giving characteristic ultra-violet absorption spectra: these include the nucleic acids and their degradation products, which absorb at $2,600 \text{ \AA.}$, ascorbic acid, which has a band at $2,650 \text{ \AA.}$, and the cell proteins, which give a maximum at $2,800 \text{ \AA.}$

An extensive study of the relation of cell-structure to metabolism has led Caspersson (1948) to the conclusion that the synthesis of proteins in the living cell is particularly related to the activity of the cell nucleus. The large nucleus

and the characteristics of the nucleolar apparatus imply a specially active protein metabolism in the nerve cell. The rate of protein synthesis and utilization varies with the state of functional activity: thus, the protein content of the cytoplasm of the motoneurons of animals exhausted by heavy muscular activity shows a significant decrease in comparison with normal resting animals (Hydén, 1947). Similarly, it is reported that the nerve cells of the cochlear ganglion show a decreased ribonucleic acid content after a period of acoustic stimulation (Hamburger and Hydén, 1945). The changes are reversible and the cells return to normal after a period of rest, but the loss is less readily made up after excessive fatigue or irritation. Nucleoprotein production can be stimulated experimentally by mild anoxia or by administering malononitrile, which appears to act by inhibiting the cyanide-sensitive systems of the cell. The Stockholm workers claim to have found polynucleotide and protein deficiencies in the cortical cells of patients suffering from various forms of mental illness, and therapeutic trials of this substance are now being carried out; but their conclusions have been questioned by Meyer (1949).

While this new method of investigation is certainly a big advance on previous histochemical techniques, the interpretation of the observed changes in the ultra-violet absorption spectra is not always easy, and it is desirable that these results should be confirmed by more directly chemical methods: but since the nerve cells constitute only a small fraction of the whole tissue, the application of the usual methods of chemical analysis would be unlikely to lead very far. In this connection it may be mentioned that a method for the preparation in quantity of isolated nuclei of cells of the cerebral cortex has recently been worked out (Richter and Hullin, 1949). The method depends on repeated fractional centrifugation after breaking up the cells by grinding the chilled tissue with ice in a solution containing sodium citrate at pH 6.0. The procedure is mild enough to avoid serious damage to many of the proteins of the cell and it has enabled the enzymes and other constituents of the nucleus to be studied. The isolated nuclei contain an active cytochrome oxidase, carbonic anhydrase, acetylcholine esterase and, contrary to the findings of some investigators who have used the Gomori histochemical method, active acid and alkaline phosphatases. These results confirm the view that the nucleus is metabolically active.

The biochemical changes found by Caspersson and his colleagues in the cell metabolites are clearly related to the changes in the Nissl bodies (described by Bodian as "nucleoprotein aggregate"), which are the most sensitive indicators of regressive changes in the nerve cell. The partial dissolution of the Nissl bodies after root section, and in other conditions, is a complex process which can hardly be expressed in simple chemical terms, for the changes follow a sequence which varies in time and in appearance from cell to cell. Gersh and Bodian (1943) conclude that the dissolution of the Nissl bodies during chromatolysis is attributable to the action of a ribonuclease, which breaks down the large ribonucleic acid molecules into smaller nucleotide fragments and thereby increases the osmotic pressure of the cytoplasm: this leads to imbibition of water, increased turgor and swelling of the cell, and a dilution of the cell contents. Hoessly (1947) has obtained a very beautiful series of photographs of unfixed

and unstained nerve cells taken with the phase-contrast microscope within 45 min. of death. The Nissl bodies are seen very clearly under these conditions, and this is taken as evidence that they are not histological artefacts, but exist as such *in vivo*. However, Spiegel *et al.* (1946) observed that the Nissl bodies, which are stable at an acid pH of 4 to 6, dissolve from paraffin sections in solutions more nearly neutral. They conclude that the Nissl bodies are made up of substances which are in solution under normal physiological conditions and precipitated by the acid liberated during post-mortem autolysis.

The biochemical changes in the neuron during regeneration have been discussed by Bodian (1947). Acid phosphatase activity is doubled during axon regeneration. The greatest increase in phosphatase activity occurs at 10 to 15 days after section in the sciatic nerve, when there is a rapid proliferation of Schwann cells. Marchent (1949), who has studied the phosphatase distribution during degeneration of the rabbit sciatic nerve, has confirmed the relation of phosphatase activity to Schwann cell proliferation: she concludes that it is not related to collagen formation. Howe and Flexner (1946) find that degeneration of motor neurones is accompanied by a decrease in the succinic dehydrogenase and cytochrome oxidase activity. Further information has been obtained about the "neuro-regenerative growth substance (NR)" which Koechlin and von Muralt (1947) believe to operate in the growth of peripheral nerve. The substance is a water-soluble, dialysable compound of low molecular weight: it can be prepared from peripheral nerve, spinal cord and brain, where it is present mainly in the white matter.

The process of collagenization of the peripheral part of a severed nerve has been investigated by Abercrombie and Johnson (1946), who have made quantitative estimations by microchemical methods of the collagen content of the rabbit sciatic nerve at different times after section. The results agree with the histological picture in showing an increase from 3.2 to 6.2 gm. collagen per cent. in 200 days. At the same time there was an increase in the quantity of other nitrogenous substances in the nerve. The process of collagen formation was not significantly affected by reinnervation. Willis (1945) has described an improved silver staining method which is believed to cause an accumulation of silver in the basic proteins such as histone and protamine in nervous tissue: in vertebrate material it picks out the axis cylinders and neurofibrillae. Berman and Nachmansohn (1946) have found that there is a rapid falling off in the choline acetylase activity of the rabbit sciatic nerve at about 72 hours after root section.

Johnson, McNabb and Rossiter (1949*b*) have studied the changes in the various lipid fractions during the course of Wallerian degeneration of the cat sciatic nerve. The first change after root section is a large increase in the water content (oedema) and a loss of neutral fat. After about 8 days macrophage action becomes prominent and a steady decrease in the cephalin and myelin lipids sets in: at the same time cholesterol esters, which were absent at first, begin to appear. The lecithin content decreases more slowly.

6. Blood-Brain Barrier and CSF

It is an old observation that the brain, in contrast to other organs, does not stain when trypan blue is administered by intravenous injection. Broman

and Lindberg-Broman (1945) have made use of this as a method of testing the action of toxic substances which affect the blood-brain barrier: they report a lowering of the resistance of the barrier and increased permeability with bile salts, hypertonic salt solutions, ethyl alcohol, acid solutions with pH below 4.0, cobra venom and bee venom. Vital red has the opposite effect of *decreasing* the permeability and attempts have been made to utilize this property therapeutically to protect the brain and spinal cord from the action of toxic substances which may be present in the circulation (Aird, 1948). Spiegel-Adolf *et al.* (1945) found that the permeability of the blood-CSF barrier, as indicated by the uranine test, was not significantly changed by ECT treatment; but they found it caused a liberation into the CSF of phosphate, potassium ions and a substance which they believed to be a nucleotide. The blood-brain barrier shows a low permeability to phosphate ions labelled with radioactive P^{32} , which pass only slowly from the blood plasma into the brain: but radioactive phosphate injected into the CSF of the subarachnoid space rapidly enters the brain. Lindberg (1949) found as much as 40 per cent. of injected phosphate organically combined and distributed throughout the substance of the brain within 2 min. of administering it by subarachnoid injection in the rat.

The question of the precise nature of the blood-brain barrier has recently been discussed by Folch (1947), who suggests that the exchange of metabolites between the blood and brain may take place at the capillary level in between the points of attachment of the "sucker feet" of the astrocytes, which thereby reduce the area of the capillary wall. He further suggests that the astrocytes may serve as nurse-cells for the neurones and that their "sucker feet" may act by absorbing glucose and other metabolites directly from the capillaries and so keep the neurones supplied. While these speculations are certainly stimulating, there is very little evidence that the astrocytes do, in fact, serve as nurse-cells in this way, and the brain capillaries have not been shown to differ markedly from those of other organs in their permeability. It would appear more probable that the fine glial membrane laid down by the astrocytes, and which completely invests the blood vessels of the brain, is responsible for the characteristic impermeability of the blood-brain barrier: it can be seen in silver-stained preparations that the astroglial membrane extends along the surface of the capillaries far beyond the points of contact of the "sucker feet."

The blood-brain barrier is apparently able to differentiate between glucose and fructose, for intravenous glucose readily passes into the brain tissue, while fructose enters only at a very slow rate. Although fructose is oxidized by brain slices *in vitro*, it is unable to maintain the electrical activity of the brain in insulin hypoglycaemia in the intact animal (Klein and Hurwitz, 1946). Klein and Olsen (1947a) estimated various metabolites in the blood and brain of the cat at different times after intravenous injection. Their observations confirmed that glucose passes rapidly from the blood into the brain, and pyruvate enters comparatively slowly: but there was no significant passage of lactate, *l*-glutamate or succinate through the blood-brain barrier. They concluded that these substances would not be expected to serve as substitutes in relieving hypoglycaemic coma. Waelsch (1949) also found that injected *l*-glutamic acid

did not enter the brain of the rat or the mouse. Glutamine is more freely diffusible, and Himwich and Himwich (1946) found evidence of some exchange of lactate as well as pyruvate between the blood and the brain in man.

The blood-CSF barrier is practically impermeable to adrenaline. Adrenaline given by subarachnoid injection causes a rapid hyperglycaemia, due apparently to a direct central action on the brain, for it does not affect the blood pressure or pulse rate (Leimdorfer *et al.*, 1947). Large intramuscular injections of penicillin or continuous intravenous infusion of amounts of the order of 100,000 units do not produce an assayable level in the CSF in the normal subject: but significant amounts can be detected under these conditions in patients with meningitis. McDermott and Nelson (1945) found that in patients with neurosyphilis, one or two large doses of 300,000–500,000 units intramuscularly produced a level of 0.02 units per ml. in the CSF in 3–4 hours: but even this low level was sufficient to produce good clinical results if maintained for a sufficiently long period, as the spirochaete is highly sensitive to penicillin. It may be noted, however, that the CSF levels are not necessarily the same as the levels obtaining in the brain, where there may be higher levels at points of local injury due to spirochaetal or other infection.

(a) *Cerebrospinal fluid*.—The methods for determining the albumin-globulin ratio in the CSF have been reinvestigated by Eeg-Olofsson (1948), who concludes that an equimolecular mixture of potassium dihydrogen phosphate and dipotassium hydrogen phosphate is superior to ammonium sulphate as a precipitant. He suggests that the presence of nucleic acid derivatives may account in part for the abnormal albumin-globulin ratios found in pathological conditions. The gold sol, mastic and other colloidal reactions of the CSF have been reviewed by Scheid and Scheid (1948), who also discuss the various modifications in the procedure which have been proposed. Brown and Baker (1947) have discussed the conditions in which the CSF protein is raised without a corresponding change in the cell count: this finding is recorded in some 60–80 per cent, of patients with Guillain-Barré syndrome.

Solomon *et al.* (1947) have reported values for the total amino-acid nitrogen and for eleven individual amino-acids in the CSF. The estimations were carried out by a microbiological method, and the individual values, which were all less than those for blood plasma, varied from $\frac{1}{4}$ to $\frac{1}{15}$ of the amounts in blood. Glutamic acid was mainly present as glutamine, with not more than 2 per cent. of the free amino-acid present. No significant difference from the normal was found in the amino-acid content of the CSF of 10 epileptics. Richter, Dawson and Rees (1949) have confirmed the relatively high glutamine content of the CSF: they found values ranging from 6.9 to 8.6 mgm. per cent. in a group of 8 schizophrenics. Harris (1945) also reported CSF glutamine values in a group of psychotic patients. It is of interest that the glutamine-glutamic acid ratio in the CSF resembles that in the blood and not that in the brain, which contains a higher proportion of the free amino-acid. Glutamine readily decomposes with the liberation of free ammonia, and this may explain the presence of the ammonia found by the older investigators in the CSF: if special precautions are taken to avoid the decomposition of glutamine, no significant amount of ammonia can be found in the CSF of normal subjects

or of epileptics, and none is liberated as a result of electrically induced convulsions (Richter, Dawson and Rees, 1949).

Spiegel-Adolf and Wycis (1946) reported the presence of an abnormal amount of a substance giving an ultra-violet absorption band at $2,650 \text{ \AA}$. in the CSF of patients with concussion. They believed the band to be due to nucleic acids or their derivatives. The substance with this absorption band was also present in the CSF of untreated schizophrenics: it was affected by ECT treatment, which also caused a liberation into the CSF of nucleases and desaminases (Spiegel-Adolf *et al.*, 1948). Hack (1947) found that the spectrum of human CSF shows a prominent band due to ascorbic acid, and Strait, Aird and Hrenoff (1947) concluded that the band at $2,650 \text{ \AA}$. should be attributed to ascorbic acid and not to nucleic acid derivatives. They confirmed this by tests depending on characteristic changes in the absorption spectra produced by acidification. The criticism has been answered by Spiegel-Adolf and Marks (1948), who consider that ascorbic acid can account for a part but not the whole of the selective absorption at $2,650 \text{ \AA}$. in the CSF in their patients.

Carrega *et al.* (1947) have reported changes in the lipid content of the CSF in epileptics: they found an increase in the phospholipids during attacks, while the fatty acids were reduced. There were no corresponding changes in the blood. According to Casaffousth (1948) the CSF phospholipids are also considerably raised in pernicious anaemia: the rise runs parallel to the clinical signs and returns to normal on treatment. Jackson and Rose (1949) report values for the histamine content of the C.S.F. in normal subjects and in patients with various cerebral abnormalities. The normal level varied from 0.2 to $3.0 \text{ \mu g.}$ histamine per 100 ml. , and there was evidence of some correlation with the cell content.

The method of injecting sterile Indian ink has been applied by Field and Briclley (1949) as a means of testing the direction of outflow of the CSF in the rabbit. A solution containing ink of particle size ranging from 0.5 to $1.5 \text{ \mu}$ was allowed to flow into the subarachnoid space after previously withdrawing fluid so that there was no rise in the intracranial pressure. Examination of animals at different times after the injection of ink revealed an extensive outflow (*a*) from the arachnoid culs-de-sac around the spinal nerve roots into the prevertebral lymph nodes, (*b*) from the arachnoid sheaths of the olfactory nerves to the lymphatic plexus of the nasal mucosa, and (*c*) from the subarachnoid sleeve of the optic nerve into the retro-orbital adipose tissue. Hassin (1948) has also carried out a series of investigations on the pathways of the CSF which agree in attaching importance to the outflow in the region of the spinal nerves.

7. Salt and Water Metabolism.

The older investigators regarded "brain swelling" as due to a swelling of the actual nerve and glial elements of the brain, but more recent work has shown that under most conditions the chief change in cerebral oedema is in the volume of the interstitial fluid, particularly of the white matter of the brain. In a study of 7 brains with unilateral lesions due to tumours or haemorrhages, Stewart-Wallace (1947) found that the oedematous tissue on the affected side

showed a marked increase in the water content (an average of 81.8 per cent. H_2O compared with 69.6 per cent. on the normal side). The increased water content was practically confined to the white matter: there was no significant difference between the grey matter of the cortex on the two sides. Some parts of the white matter appeared more liable to oedema than others, and it was particularly marked in the *centrum ovale*. There was a large increase in the sodium and chloride content of the oedema tissue, with relatively little change in the potassium or phosphate, which are mainly intracellular. The increase was thus restricted to the extracellular ions and it could be calculated that the oedema fluid must contain practically the same salt content as a normal serum filtrate. Stewart-Wallace concluded that, as in other parts of the body, the oedema fluid associated with cerebral tumours and haemorrhages is an extracellular effusion from the blood plasma. There is no significant swelling of the neurones or glial cells until the increase in brain volume exceeds about 5 per cent.

The normal salt and water content of the brain, as of other tissues, is controlled partly by the anterior pituitary acting through the adrenal cortex, and partly by the posterior pituitary through chemoceptors sensitive to osmotic pressure and believed to be situated in the supraoptic nucleus (Verney, 1946). The water content of the brain is also affected by oestradiol injection. Douglas *et al.* (1948) suggests that the effects of oestradiol in altering the threshold of rats to sexual stimulation and in facilitating related patterns of response may be attributable to specific changes in the hydration of the brain. Klein and Nunn (1945) have described a case of manic-depressive psychosis, with weekly cycles characterized by water and salt retention during the depressed phase, and release during the manic phase. Mental symptoms associated with salt retention have been described in "premenstrual tension," but a considerable degree of salt retention can occur without manifest mental symptoms and Hess (1946) reports two cases which show this. With a daily intake of 17 gm. sodium chloride only 1-2 gm. were excreted: but large amounts were excreted at intervals. There was no evidence of any renal abnormality and the condition appeared to be of diencephalic origin.

Gellhorn and Ballin (1946) have studied the sequence of EEG changes produced by water intoxication in the rat. Water was given by intraperitoneal injection (50 ml. water per kg. every 30 min.). There appeared slow waves at 1-3 c./sec., which slowly decreased in amplitude until there was finally a disappearance of cortical potentials as coma set in and the animals died. Seizure patterns of various types were also seen to occur and in some cases convulsions were observed. Swinyard *et al.* (1946) have studied the effect of hydration in lowering the ECT threshold.

Salt depletion was a common cause of psychological disturbances in troops in the Middle and Far East during the war, and the term "tropical neurasthenia" has been widely used to cover this condition (Marriott, 1947). Lassitude, apathy, weakness, headaches, giddiness and cramps are common symptoms, and gastro-intestinal symptoms, such as vomiting, anorexia and diarrhoea, may produce a vicious circle by further reducing the body's supply of salt, so that the period of debility is prolonged.

Stone and Shapiro (1948) have determined the sodium and potassium content of ultrafiltrates prepared from homogenized brain tissue. Their figures indicate that these two kations behave differently in that the sodium ions diffuse out freely, while some 25 per cent. of the potassium ions remain in the residual solids in an apparently non-diffusible form. They conclude that this part of the potassium is combined in the brain in the form of a complex. In a study of the state of combination of the kations of the rat brain, Epshtein (1948) finds that there are 203-209 milliequivalents of base per kg., while the anions are made up as follows: chloride 36.2, phosphate 16.1, bicarbonate 12.5, lipid 67.5, amino-acids 19.2, lactic acid 7.0, ascorbic, β -hydroxybutyric and acetoacetic acids 3.0, and proteins and other unknown anions 42.4. The acids thus constitute the chief acidic component of the brain.

In biochemical work on the brain it is often necessary to know the blood content of the brain, since the blood accounts for a significant part of the salts and other metabolites found in the tissue. Gibson *et al.* (1946), in a very outstanding piece of work, have determined the blood content of the dog brain by using radioactive tracers in combination with the dye method. For this purpose they used red blood corpuscles tagged with radioactive iron and the iodine isotope in the blood plasma. Their mean figures for 7 animals, on pieces of brain tissue free from large blood vessels, indicated a blood content of 1.3 ml. per 100 gm. brain tissue. The content of red blood corpuscles was 0.6 ml. per 100 gm. tissue.

8. *Acetylcholine and Choline Esterases.*

(a) *Acetylcholine.*—Acetylcholine is present in the tissues mainly in the form of a complex which liberates free acetylcholine ions when the tissues are extracted with deproteinizing reagents. Abdon (1945) has shown that the complex can be extracted from muscle with alcohol and precipitated by barium salts. It is unstable to heating or to treatment with acids, but it is relatively stable at pH 4. A complex with similar properties can be extracted from brain and peripheral nerve (Welsh and Prajmovsky, 1947). A part of the tissue acetylcholine goes into solution if the tissue is extracted with water or saline containing eserine to inhibit the choline esterase. About 10-20 per cent. of the total acetylcholine can be extracted in this way, and this fraction has been regarded by some investigators as being present in the tissues in the free state; but this view is unconvincing, for it is hard to believe that as much as 20 per cent. of the total acetylcholine can evade the action of choline esterase for very long. This "free acetylcholine" is also ill-defined, for the amount extracted by saline varies with the time and conditions of the extraction: it would appear more likely that there is a partial breakdown of the complex during extraction under these conditions. Prajmovsky and Welsh (1948) reported that more "free acetylcholine" can be extracted from the rat brain after convulsions: but convulsions also affect the amounts of lactic acid and other acidic metabolites in the tissue. Hobbiger and Werner (1948) conclude that free acetylcholine is in equilibrium with two forms of bound acetylcholine in the brain.

The acetylcholine content of the brain increases with age. Freedman and Himwich (1948) found four times as much in the brain of the adult rat as in

the brain of newborn rats. Such estimations are usually made on trichloroacetic acid extracts of the tissues, and Perry (1949) has recently shown that acetylcholine is inactivated at an appreciable rate at room temperature by trichloroacetic acid at concentrations commonly used for extracting tissues. He finds the optimum time of extraction to be about 2 hours. In tissues which have been frozen in liquid air the cells are broken up and a high yield of acetylcholine can be obtained by extraction for less than half an hour (Crossland and Richter, 1950).

There have been a number of investigations of choline acetylase, the enzyme which synthesises acetylcholine. It is water-soluble and can be extracted from acetone-dried preparations of mammalian brain and other tissues. Feldberg and Mann (1946) showed that the activity of the system is greatly increased by the addition of ATP, citrate and an activator which can be extracted from brain and other tissues. Lipton and Barron (1946) report that at least 5 components are required for full activity: these are choline, potassium, ATP, a coenzyme present in boiled extracts of animal tissues and an oxidizable substrate such as citrate, cis-aconitate or acetoacetate. Comline (1947) has found that the system is activated by a flavine-adenine-dinucleotide present in the tissues: Lipmann *et al.* (1947) report that the activator is a derivative of pantothenic acid. The enzyme is present in sympathetic ganglia and along the whole course of the motor nerve fibres. Feldberg and Vogt (1948) have investigated the distribution of choline acetylase in different parts of the mammalian central nervous system. They found that the ability to synthesize acetylcholine ran parallel to the normal acetylcholine content, from which they concluded that it gives a measure of the proportion of cholinergic fibres in the region. They obtained evidence that there is an alternation of cholinergic and non-cholinergic fibres in the neuronal chains constituting the normal afferent and efferent pathways in the brain and spinal cord. References to further work on the choline acetylase are given by Jukes (1947), Hobbiger and Werner (1949), and Nachmansohn and Weiss (1948).

Acetylcholine is hydrolysed by the choline esterases, of which two main types have been recognized. The varying nomenclature given to these enzymes by different investigators has given rise to a good deal of confusion. The two types of choline esterase are in fact quite different in their properties, in their distribution and in their functions. For the sake of clarity they are described here as acetylcholine esterase and butyrylcholine esterase respectively.

(b) *Acetylcholine esterase*.—This is the so-called "specific" or "true" choline esterase, which is present in high concentration in the brain and nervous tissue and in human erythrocytes. It was formerly described as "specific" since it was found not to hydrolyse substrates such as methyl butyrate, tributyrin or benzoylcholine: but it has recently been shown that, besides hydrolysing acetyl- β -methylcholine, it hydrolyses triacetin and other aliphatic acetate esters (Bodansky, 1946; Holton, 1948; Adams, 1949). The enzyme can no longer be described as strictly specific; but it hydrolyses acetylcholine more rapidly than any other known substrate, and it has a characteristically low Michaelis constant with acetylcholine, which indicates that it is active at very low acetylcholine concentrations. From these facts and from its

distribution in nervous tissue, which contains acetylcholine, it is reasonable to conclude that the hydrolysis of acetylcholine is its main physiological role. The name acetylcholine esterase, which has now been adopted by Nachmansohn and a number of other investigators, appears appropriate.

Nachmansohn has attached some importance to the localization of acetylcholine esterase at the surface of the nerve cell, where it is suitably situated for the inactivation of acetylcholine. This may be true for the squid axon, but it does not appear to be true for the mammalian brain, in which a considerable proportion of the acetylcholine esterase is present in the cell nucleus (Richter and Hullin, 1949). Birkhäuser (1941) has confirmed the observation of earlier workers that acetylcholine esterase is present in significant concentration in the CSF (see Augustinsson, 1948). The activity in the CSF is considerably lower than in the brain and spinal cord, but he obtained very high activities in the CSF of patients with meningitis. The activity in the CSF of schizophrenics gave a mean of 19.4 units/ml., which was slightly but significantly higher than the normal mean of 14.0. Glasson and Mutrux (1946) showed that the CSF contains an *ali*esterase as well as an acetylcholine esterase. This would agree with the observations of Reiss and Hemphill (1948).

A great deal of work has been carried out on the action of inhibitors, and particular interest attaches to the substance diisopropyl fluorophosphate, which is commonly known as "DFP." The unusual properties of this compound were discovered as a result of the investigation of toxic substances suitable for chemical warfare, and, according to Dixon and Needham (1946), this is the most powerful and most specific enzyme inhibitor known: it inhibits the acetylcholine esterase and butyrylcholine esterase irreversibly in concentrations as low as 1×10^{-10} molar. Small doses administered to 8 human volunteers produced contraction of the pupils and a subjective feeling of tightness in the chest: occasionally there was increased nasal secretion, nausea and salivation. The symptoms observed in experimental animals indicate a primary action on the central nervous system. A dose of 1 mgm./kg. is lethal in the rabbit; but 0.3 mgm./kg. produces increased reflex activity, muscle tremor and sometimes convulsions. With this dose most animals survive, and since this amount is sufficient to cause a very considerable inhibition of the brain acetylcholine esterase (Mazur and Bodansky, 1946), it has been concluded that the acetylcholine esterase is not of vital importance in the mechanisms of nervous transmission. However, Nachmansohn and Feld (1947) were able to show that significant amounts of acetylcholine esterase are always present in the brains of animals which survive: they found it absent only in those which died. Comroe *et al.* (1946) have tried DFP as an acetylcholine esterase inhibitor in the treatment of patients with myasthenia gravis and they report that it produces some improvement, but less than can be obtained with neostigmine. It also caused undesirable side-effects, such as nausea and vomiting.

The inhibitory action of eserine on the acetylcholine and butyrylcholine esterases is reversible, but the inhibition by DFP and by tetraethyl pyrophosphate (or "TEPP") of these enzymes is irreversible, and therefore depends on the time the enzyme and inhibitor are in contact with each other.

The inhibition by these irreversible inhibitors is also reduced if the enzyme substrate, acetylcholine, is present at the same time (Augustinsson and Nachmansohn, 1949). Adams and Thomson (1948) have found that $\beta\beta'$ -dichlorodiethyl-N-methylamine is a selective inhibitor for the acetylcholine esterase, but not for the butyrylcholine esterase, and des Marais (1947) has reported that of the two enzymes only the acetylcholine esterase is activated by folic acid.

(c) *Butyrylcholine esterase*.—This is the so-called “unspecific” or “pseudo-” choline esterase which is present in the blood plasma, liver, and in bitches' colostrum, but not in considerable amount in the brain or spinal cord. This enzyme may have to do with nutrition and possibly with liver function, but there is no evidence that it has any direct connection with the action of the nervous system. It hydrolyses methylbutyrate, tributyrin and other aliphatic butyryl esters at a relatively high rate. It is also more active towards butyrylcholine than towards acetylcholine. The high Michaelis constant with acetylcholine indicates that it has little activity towards acetylcholine at the low concentrations normally found *in vivo*, and this explains why acetylcholine can remain in the blood plasma for a considerable time without being rapidly inactivated by the “serum choline esterase.”

The butyrylcholine esterase is the enzyme mainly responsible for the hydrolysis of tributyrin by human serum, and in this role it was known originally as the “serum lipase.” The older investigators recognized the relation of this enzyme to nutritional factors and observed the falling off in activity in cachexia due to tuberculosis and other conditions. Later, when Stedman found an enzyme in serum which hydrolysed acetylcholine, he renamed this enzyme “choline esterase,” a name which the American investigators contracted to “cholinesterase.” With the discovery that the serum choline esterase was different from the acetylcholine esterase of nervous tissue it became necessary to differentiate between them, and the terms “unspecific” and “pseudo-” were applied to the serum enzyme. The term “unspecific” is no longer applicable, since neither enzyme is strictly specific, and the designation “pseudo-” has been strongly criticized: the serum choline esterase is in fact a true enzyme and it does not belong to the class of pseudo-enzymes, such as the pseudo-peroxidases, which are recognized by the biochemist. The finding that the serum choline esterase is more active towards butyryl esters than towards the corresponding acetyl esters suggested the name butyrylcholine esterase for this enzyme: this name has not yet been generally adopted, but it was discussed and found some acceptance at the recent International Congress of Biochemistry (Whittaker, 1949). The name would appear appropriate in that it expresses the substrate class to which the enzyme is most active, and it distinguishes this enzyme from the esterase which is believed to have the physiological function of inactivating acetylcholine.

The activity of the butyrylcholine esterase of the serum has recently been shown to fall in starvation and, since the change is reversible, it can serve as an index of the nutritional level (McCance *et al.*, 1948). This agrees with the older observations that the activity is lowered in cachexia and in prolonged catatonic stupor: it also suggests that the increase in activity in schizophrenics produced by insulin treatment may be attributable to the improvement in

the nutritional state. McCance *et al.* (1949) have studied the changes in the butyrylcholine esterase of the serum and colostrum in various animals. The activity in the serum of newborn puppies was 35 units; they found that this rose to 1,000 units in a few days, after which it gradually fell again to about 50 units. The rapid rise in the activity did not occur in puppies reared on dried milk, which indicated that the effect might be due to the mother's colostrum. Estimations on bitches' colostrum gave butyrylcholine esterase activities of the order of 6,000 units, which gives confirmation for the view that the butyrylcholine esterase can enter the serum in this way. It has been known for some time that the activity of this enzyme is related to liver function, since low activities are found in patients with liver disease, and recent work has supported the view that the butyrylcholine esterase is produced in the liver and enters the blood plasma from this source. The activity is also influenced by endocrine factors: thus, the activity in the plasma of the rat varies with the sex, and is greatly affected by the administration of oestradiol and testosterone in castrated animals (Sawyer and Everett, 1947). The activity is also affected by the administration of thyroxine and thiouracil (Hawkins *et al.*, 1948). Stonor and Wilson (1943) found no change with exercise in the butyrylcholine esterase activity of the blood of the arm after occluding the circulation; but this would not be expected if the enzyme is produced in the liver, and Brecht (1947) has confirmed the rise in the activity in the serum in exercise when the circulation is maintained intact. A good account of the literature on this enzyme is given in the monograph by Augustinsson (1948).

9. Adrenaline and Histamine.

(a) *Adrenaline*.—An advance has been made by the demonstration that the sympathomimetic substance of the adrenal gland is not pure adrenaline but a mixture of adrenaline and nor-adrenaline (arterenol). This compound resembles adrenaline fairly closely in many of its physiological properties, and it is similar chemically except in that it has an amino-group instead of a methyl-amino-group on the side-chain. Nor-adrenaline has now been isolated in the pure state from cattle adrenals, where it is present together with adrenaline in the approximate ratio of 1:4 (Holton, 1949; Bülbring and Burn, 1949; Bergstrom, 1949).

In an investigation of the source of adrenaline in the body, Gurin and Delluva (1947) administered to rats phenylalanine labelled with radioactive C^{14} in the carbon atom in the α -position or in the carboxyl group. The phenylalanine tagged in the α -position was converted into radioactive adrenaline containing C^{14} in the terminal carbon atom of the side-chain. The results give convincing evidence that adrenaline is derived from phenylalanine by a process of oxidation, decarboxylation and methylation. Nor-adrenaline may thus be an intermediate from which adrenaline is derived by methylation.

The inactivation and detoxication of adrenaline and other pressor amines in the body was very adequately reviewed by Hartung (1946). Beyer and Shapiro (1945) have confirmed the inactivation by conjugation in the tissues, and they found that as much as 83 per cent. of adrenaline administered to dogs was recovered in the urine in the form of the sulphoconjugate. Holtz *et al.*

(1947) have reported the presence of a small amount of conjugated pressor substance in the urine of normal men: it is apparently a mixture of adrenaline, nor-adrenaline and hydroxytyramine. The daily excretion is equivalent to 0.1-0.15 mgm. of adrenaline and they found that the amount excreted was increased by muscular work. Bacq (1949) in a review of the general metabolism of adrenaline, has also reported a number of new observations on the inactivation of adrenaline in the tissues: he noted a partial conjugation of adrenaline administered by intravenous injection in the dog. Adrenaline is also excreted, to a limited extent, unchanged in the urine under certain conditions in the dog and the cat.

There have been several reports of a direct central action of adrenaline on centres in the brain and spinal cord. Stavsky (1947) found both stimulant and depressant actions on spinal cord neurones. Leimdorfer *et al.* (1947) observed a rapid rise in the blood sugar after intracisternal injection of small amounts of adrenaline which were insufficient to produce a general circulatory response and which apparently acted directly on centres in the brain. Cohn and Needham (1948) have found that the glucose utilization of muscle from rats previously injected with adrenaline was some 30 per cent. less than that of normal controls, and they suggest that this may be a part of the mechanism of adrenaline hyperglycaemia. No direct action of adrenaline on muscle extract could be demonstrated and they conclude that adrenaline acts indirectly through other hormones affecting the phosphorylation of glucose by the hexokinase system.

Gaddum, Peart and Vogt (1949) have reinvestigated the methods available for the estimation of adrenaline in the blood. The five most satisfactory preparations were the rat uterus and colon, the rabbit ear, and the cat spleen and denervated nictitating membrane. Attempts to apply these methods directly to blood showed that the result is vitiated by the release of interfering substances in the blood. This could be avoided by collecting the blood with much heparin in cooled tubes coated with silicone, and rapidly centrifuging to remove the red blood corpuscles. If these precautions were used, and parallel assays by these five methods were carried out, it was possible to estimate adrenaline at concentrations down to 10^{-8} or nor-adrenaline at 10^{-7} . The problem of finding a simple method for the determination of blood adrenaline has not yet been solved.

(b) *Histamine*.—The view that histamine may act as a chemical mediator of cutaneous pain is supported by recent work of Rosenthal and Sonnenschein (1948), who have found that painful sensations can be detected on injection of as little as 0.1 ml. of a 10^{-18} solution of histamine into the skin. Dekanski (1945) has studied the effects of burning on the histamine content of the mouse. Some 75 per cent. of the total histamine is in the skin, and a rapid liberation of histamine was produced by burning anaesthetized mice with hot water, so that the total histamine content was doubled in 10 minutes. The excess of histamine was mainly excreted in the next 48 hours, if the mouse survived. He concluded that the amount of histamine released can account for the local response at the site of burning, but it cannot easily account for the general circulatory changes in shock.

Histamine is present in significant amounts in the brain (Cicardo and Stoppani, 1949). The production of anaphylaxis of the brain has been discussed by Ferraro (1945), who obtained experimental anaphylactic reactions in the monkey by repeated intravenous injection of egg-white, followed by injection of a small amount directly into the brain. Monkeys treated in this way died within 15 hours with general signs of collapse. Histological examination of the brain showed a definite inflammatory reaction with necrosis at the point of injection and oedema of the surrounding tissue, but no evidence of any infective agent. There were petechial haemorrhages throughout the grey and white matter of the brain. According to Poupa (1948) the action of histamine on the blood vessels of the brain is not uniform: the arterioles of the cerebral cortex are constricted, while the arteries of the base are dilated by histamine in the rabbit. These effects are prevented by benadryl.

Quantitative methods for the estimation of histamine in the urine have been developed by Anrep *et al.* (1944), who showed that orally-administered histamine is eliminated by this route in man. A small amount is present in the urine under normal conditions, partly conjugated and partly free, and the amount is increased after eating meat. Histamine given by subcutaneous injection is found to the extent of 85–100 per cent. in the urine in the dog. Kapeller-Adler (1949) has described the preparation and properties of a purified histaminase from hog kidney: it appears to be a flavoprotein with a flavin-adenine-dinucleotide as the prosthetic group. She has also obtained a rapid chemical method for the estimation of histaminase activity in the serum: the results by this method show good agreement with those obtained by biological methods.

It is well established that a number of toxic substances, such as peptone, animal venoms, etc., produce the triple response due to histamine liberation when injected into the skin. MacIntosh and Paton (1949) have now found that a number of relatively simple basic substances act in part by causing a liberation of histamine from the tissues, which may occur particularly from the skin and the liver. This accounts for some of the depressor effects of the diamines, curare and the morphine group of alkaloids. It was believed, until recently, that the rash produced on the skin by the sting of the nettle was brought about by some unknown toxic substance which released histamine from the epithelial cells; but Emmelin and Feldberg (1947) have now shown that the poisonous fluid of the nettle hair contains a mixture of histamine and acetylcholine in high concentration. The histamine, present in a concentration of about 0.1–0.2 per cent., is responsible for the triple response and the itching sensation, while the combination with acetylcholine, present in 1 per cent. or more, causes the painful burning sensation of the nettle sting.

10. *Intermediary Metabolism.*

(a) *Carbohydrate utilization.*—Progress has been made in the elucidation of the intermediary reactions by which the energy obtainable from the oxidation or glycolysis of glucose is made available for the functional activity of the cell. The first step in the chain of reactions is the phosphorylation of glucose catalyzed by hexokinase, and evidence is collecting which suggests that this reaction

is under direct hormonal control (Cori, 1945). Colowick, Cori and Slein (1947) reported an inhibition of hexokinase by pituitary anterior lobe fractions *in vitro*: adrenal cortical extracts also inhibited, while insulin increased the phosphorylation of glucose by reversing the inhibition. Beef brain extracts gave an inhibition of 30-75 per cent. in the rate of phosphorylation. With a partially-purified preparation of hexokinase from beef brain they were able to show that the phosphorylation of glucose occurs directly in the 6-position without the intermediate formation of glucose-1-phosphate. Adrenal cortical extract had no effect unless a pituitary fraction was also added. The demonstration of reproducible *in vitro* effects by these various endocrine principles represents a big advance and, although there has been some disagreement over a few points, the main results appear to have been confirmed (Smith, 1949). In agreement with these observations, Reiss and Rees (1947) were able to show an increase of 37-140 per cent. in the brain hexokinase activity in hypophysectomized rats. Adrenalectomy also produced an increase, but, contrary to Colowick, Cori and Slein, they found an inhibition of hexokinase by adrenocorticotrophic hormone. The hexokinase reaction is also affected by substances present in human blood plasma and corpuscles (Weil-Malherbe, 1948).

Coxon, Liébecq and Peters (1949) have shown that the addition of co-carboxylase *in vitro* increases the production of citrate and α -ketoglutarate from pyruvate in dialyzed homogenates of B₁-avitaminous pigeon brain. The system contained magnesium ions, fumarate and adenine nucleotide. They conclude that oxidative decarboxylation to form a 2-carbon fragment is a definite step in the metabolism of pyruvic acid and that the tricarboxylic acid cycle operates in the brain. Confirmation of this view has been afforded by the observation that fluoracetate injected in the rat causes a large accumulation of citrate in the brain and other tissues *in vivo* (Buffa *et al.*, 1949).

Cozymase is present in nervous tissues, and Anfinsen (1944) has shown that in the bovine retina it is concentrated in the synaptic regions, which also contain the highest concentration of acetylcholine esterase. McIlwain and Rodnight (1949a and b) have investigated the enzyme system in the brain, which inactivates cozymase and coenzyme II. This enzyme, which is very active in the brain and more active in the white matter than in the grey, splits off ribose liberating free nicotinamide. Since it has no action on dihydrocozymase, it may be expected to affect the oxidation-reduction potential of the tissue, and it is suggested that this enzyme may thereby act as a controlling mechanism for carbohydrate metabolism. Racker and Krimsky (1945) showed that glycolysis by mouse brain is inhibited by a diphosphonucleotidase which can be antagonized by nicotinamide and which acts by preventing the utilization of triosephosphate. Utter, Wood and Reiner (1945) also observed that this nucleotidase inhibited by nicotinamide is the glycolytic "inhibitor" found by the older investigators in brain extracts and homogenates. They showed that high rates of glycolysis could be obtained with cell-free extracts and homogenates of the brain and spinal cord by the addition of nicotinamide, coenzyme I, magnesium ions, hexosediphosphate and ATP. Judah and Williams-Ashman (1949) have reported the action of a number of dyes and other inhibitors which affect the coupling of oxidation and phosphorylation reactions: their

results indicate that the aerobic inhibition of glycolysis is not due to the lowering of the concentration of inorganic phosphate. Dixon (1949) suggests that potassium ions, which inhibit glycolysis at low concentrations, may act as an inhibitor of glycolysis *in vivo*.

Recent results, obtained by Meyerhof and his collaborators, on glycolysis in brain homogenates and extracts have recently been summarized (Meyerhof, 1948). They attribute a controlling role to adenosinetriphosphatase and ATP. Meyerhof and Wilson (1948) showed that glucose is metabolized faster than fructose in rat-brain slices, homogenates and extracts, provided that the ATP concentration is sufficiently low: but the difference disappears if ATP is added. A possible explanation is that there are two enzymes present, a glucokinase and a fructokinase, which have different affinities for ATP. The characteristic differences usually seen in the behaviour of brain slices, homogenates and extracts depend largely on the fact that adenosinetriphosphatase is structurally bound, so that it is relatively inactive in brain extracts: conversely, the ATP level is normally higher in extracts than in brain slices or homogenates, from which it rapidly disappears. A number of further studies on the adenosinetriphosphatase of mammalian and invertebrate nervous tissues have been reported (Moog, 1947; Libet, 1948): rat brain also hydrolyses inorganic pyrophosphate in the presence of magnesium ions (Gordon, 1949). In a study of the inhibition of glycolysis in mouse-brain slices by partially purified virus preparations, Racker and Krimsky (1948) found that the inhibitory action could be traced to the iron content of their preparations. Glycolysis of glucose, but not of hexosediphosphate, was inhibited by previous incubation of the slices with ferrous salts. The inhibitory effect of ferrous salts was localized to the coupled phosphorylation linked with the oxidation of phosphoglyceraldehyde: they suggest that ferrous ions inactivate the phosphoglyceraldehyde dehydrogenase, addition of which restored the glycolytic activity of the system. Further work on carbohydrate metabolism is to be found in the reviews by Wood and Lorber (1949), Vennesland (1948) and Stetten (1947).

(b) *Glutamic acid*.—Goodman *et al.* (1946) and Wagner (1947) have been unable to confirm the anticonvulsant action reported for glutamic acid, and several investigators have failed to confirm the effect reported on intelligence in the rat (Marx, 1948; Hamilton and Maher, 1947; Stellar and McElroy 1948). Weil-Malherbe (1949) could find no evidence for any action of glutamic acid in relieving hypoglycaemic coma other than the unspecific effect in raising the blood glucose through adrenaline release: this effect, which could be imitated by injecting adrenaline, is not specific for glutamic acid, since it is also shown by glycine, phenylalanine and other amino-acids. However, claims for clinical effects of glutamic acid continue to be made (Zimmerman *et al.*, 1948; Meyer-Gross and Walker, 1949). Davenport and Davenport (1948) noted that glutamic acid raised the ECT threshold and reduced cerebral irritability in pyridoxin-deficient rats, and Spangler (1945) found that daily administration of *dl*-glutamic acid produced a significant decrease in the pH of the urine, which fell to pH 4. Sapirstein (1943) reported that glutamic acid increased the resistance of animals to convulsions induced by injection of ammonium chloride.

Whatever the outcome of the various claims for clinical effects, and it would be surprising if they proved to be entirely without foundation, glutamic acid remains a metabolite of unusual interest to the biochemist. Stern (1948) has found that *l*-glutamic acid accumulates against a concentration gradient in brain slices suspended in saline containing glucose. The concentration in the slices may reach 20 times that in the external medium: the effect depends on the presence of oxygen and an oxidizable substrate to supply energy. There was no appreciable accumulation under anaerobic conditions. *d*-Glutamate was converted into *l*-glutamate by the brain slices (Stern *et al.*, 1949). They suggest that the accumulation of glutamate against a gradient may account for a part of the large energy requirement of the brain. ATP abolished the inhibition of brain glycolysis by glutamate, and they suggest that glutamate inhibits glycolysis by reacting with ATP to form glutamyl- γ -phosphate: the removal of ATP by this reaction would account for the slowing down of glycolysis. Krebs and Eggleston (1949) have pointed out that the glutamate-transporting mechanism can account for the accumulation of kations such as potassium in the nerve cell. Stern *et al.* regard the cell membrane as freely permeable to glutamic acid, but the rate at which glutamic acid passes from the blood into the brain appears to be relatively slow *in vivo* owing to the blood-brain barrier (*q.v.*). Glutamic acid administered by injection does not produce a significant increase in the glutamate content of the brain in experimental animals; but this might be because the glutamic acid entering the brain is rapidly metabolized. Dawson (1949) has shown that the glutamic-acid content of the rat brain falls to a low level in insulin hypoglycaemia, which suggests that the brain can utilize glutamic acid if the glucose supply fails, but the fall might also be attributed to the inability of the energy-supplying mechanisms to maintain the normal concentration gradient between the brain and the plasma.

ATP can serve as an energy-donor for the synthesis of glutamine from glutamic acid and ammonia (Speck, 1947). Preparations from acetone-dried sheep brain are active in the presence of added magnesium ions, and inorganic phosphate is liberated. Hydroxylamine can be used in the place of ammonia and glutamyl phosphate is suggested as a possible intermediate (Elliott, 1948). Glyconeogenesis from glutamic acid and other amino-acids is impaired in the adrenalectomized rat (Ashby, 1949). The brain and other tissues can synthesize glutamic acid from α -ketoglutarate and ammonia by reductive amination coupled with the oxidation of *l*-malate or of α -ketoglutarate itself (Krebs, Eggleston and Hems, 1948). The same authors report a series of estimations of glutamic acid and glutamine in different organs of a number of mammalian species: the highest glutamic acid figures are for cerebral cortex, heart muscle, spleen and thymus. A highly specific method for estimating glutamic acid in the tissues is given by Krebs (1948), who employs the specific decarboxylase in washed suspensions of a certain strain of *Clostridium Welchii*: the carbon dioxide liberated is determined manometrically with the Warburg apparatus. Prescott and Waelsch (1947) report values for the glutamic acid and glutamine content of the blood. Other work in this field has been recently reviewed by Waelsch (1949).

(c) *Lipids*.—A new series of determinations of the lipid fractions in the white and grey matter of the brain of the cat, dog, beaver and man have been reported (Johnson, McNabb and Rossiter, 1948*a* and *b*; 1949*a*). Grey matter contains a higher proportion of phospholipids, while white matter resembles peripheral nerve in containing relatively more cerebroside, cholesterol and sphingomyelin, which are therefore believed to be the main constituents of myelin. This was confirmed in a study of the changes in the lipids of the brain during the period of myelination in the infant. The white matter of the infant brain, before myelination, differs greatly from that of the adult in lipid content and shows relatively little difference from grey matter. Elkes *et al.* (1949) have studied the X-ray diffraction patterns of the myelin of frog sciatic and other nerves. Observations on the changes produced by various solvents agree with the view that myelin should not be regarded as a simple lipid mixture, but as a complex structure of alternating lipid and lipoprotein units. Alsterberg (1945), who has studied by histochemical methods the distribution of lipids in nerve, reports that the cholesterol and cerebroside are mainly present in the myelin sheath, while lecithin and sphingomyelin are in the axis cylinder. Sphingomyelin and protein-bound cephalins may be in the axilemma. Glial structures contain serine cephalin and inositol cephalin.

The inositol-containing phosphatide of brain cephalin has now been isolated. This compound, named *diphosphoinositide*, contains glycerol, fatty acids and inositol metadiphosphate as constituents. It contains two atoms of P per molecule of fatty acid. Methods for the complete separation of the brain cephalin fraction into phosphatidyl serine, phosphatidyl ethanolamine and the new diphosphoinositide have now been worked out (Folch, 1946). Dawson and Richter (1949) have studied the phospholipid metabolism of the mouse brain *in vivo* by the use of radioactive phosphorus as a tracer. The rate at which P^{32} is incorporated into the phospholipids indicates a surprisingly high metabolic activity for substances which have been regarded as structural elements of the cell: the rate corresponds to a complete exchange of the total phosphorus present in the fraction in 70 hours. The rate of phosphorus exchange varies with the physiological state: it is reduced in anaesthesia, insulin coma and ECT treatment. Klenk (1948) has reported the presence in brain of a new group of acetal phosphatides, in which two hydroxyl groups of the glycerol molecule are linked with the carbonyl group of an aliphatic aldehyde to form an acetal with a heterocyclic ring. He isolated a small amount of stearal as the oxime, but the main bulk of the aldehydes formed an oil which he could not crystallize. Oster (1946) has isolated and identified palmital and stearal from the white matter of the brain: he also noted the presence of other aldehydes not yet identified, which give alcohol-soluble dimethylacetals.

Klenk and Leupold (1944) have described the purification of the cerebroside of human brain by chromatography in pyridine solution on alumina columns. By this method they obtained products which were completely phosphorus-free. Hydrolysis yielded 63 per cent. nervonic acid, 17 per cent. *n*-hexacosenic acid, 9 per cent. stearic acid, 6 per cent. of a C_{20-22} acid, 3 per cent. palmitic acid and 2 per cent. of higher acids. They conclude that hitherto unknown cerebroside must be present in the brain. Carter *et al.* (1947) have

isolated dihydrosphingosine from the cerebroside fraction of beef brain and spinal cord. The sphingolipids were separated by fractional crystallization of their acetyl-derivatives from methanol after acetylation with acetic anhydride in pyridine solution. Carter *et al.* (1947b) have reinvestigated the constitution of sphingosine: they found that the old formula of Klenk and Diebold is incorrect and that the amino-group is on the 2-carbon atom. The corrected formula for sphingosine is 1,3-dihydroxy-2-amino-octadecene-4. The constitution of dihydrosphingosine is similar except for the saturation of the double bond.

Brain sphingomyelin has also been shown to contain both saturated and unsaturated sphingosines. Acid hydrolysis of a purified sample yielded stearic, nervonic and lignoceric acids in the approximate molecular ratios of 2 : 2 : 1, in addition to sphingosine and dihydrosphingosine sulphates (Thannhauser and Boncoddo, 1948). The same investigators have isolated and identified hydrolecithin (dipalmityl lecithin) from beef brain.

II. Chemical Pathology.

Reference has already been made to a number of investigations which have a bearing on the chemical pathology of the nervous system, but there are a few further studies which may be included more conveniently under this heading. The difficulties of investigation in this field are increased by the lack of satisfactory objective diagnostic criteria and by the special difficulties inherent in working with human subjects. For this reason reports of pathological abnormalities can rarely be accepted as of general application until they have been critically examined and confirmed in two or more different laboratories. Progress is therefore inevitably slow.

(a) *Oligophrenias*.—In a useful review of *phenylketonuria*, Penrose (1946) has pointed out that there are a number of points which still await biochemical investigation. It has not been established where the phenylpyruvic acid comes from, or how the mental and physical abnormalities are related to the metabolic defect. It is known that the blood phenylalanine is greatly raised, while there is little or no phenylpyruvic acid in the blood of phenylketonurics: in the urine there is found a large amount of phenylpyruvic acid and the phenylalanine is also slightly raised (Dann, Marples and Levine, 1943). The hypothesis was put forward by Fölling, Mohr and Rund (1945) that the essential error consists in the abnormal racemization of phenylalanine in phenylketonurics, so that the naturally occurring *l*-form is converted into the *d*-form, which is deaminated in the kidney and subsequently excreted as phenylpyruvic acid. This would agree with the fact that administration of *d*-phenylalanine causes an excretion of phenylpyruvic acid in normal subjects; but it does not explain the accumulation of phenylalanine in the blood of phenylketonurics. Jervis (1947) has now ascertained a further fact in showing that administration of phenylalanine to normal subjects causes an apparent rise in the blood tyrosine level, due to oxidation of the benzene ring, but this effect is absent in phenylketonurics. He concludes that the inability to oxidize phenylalanine to tyrosine is the essential metabolic error in the phenylketonuric. This would explain the abnormal accumulation of phenylalanine in the blood and also

the raised excretion of both phenylalanine and phenylpyruvic acid in the urine.

Erythroblastosis foetalis, associated with sensitization by rhesus agglutinogens, occurs in about 1 in 150–200 births, and the suggestion that this may give rise to the development of mental defect has aroused a good deal of interest. Penrose (1945) indicated that caution is needed in accepting this conclusion on the present evidence, but Snyder and Schonfeld (1945) found, in an examination of 113 feeble-minded children, that 16 were Rh + ve from Rh – ve mothers, which is considerably more than the normal expectation. In a more recent follow-up of 6 children treated by blood transfusion for icterus gravis, Third (1946) found one imbecile and two probably mentally defective.

Strauss *et al.* (1947), in a study of the changes in the lipids in gargoylism, found an increase in the neutral fat in the lymph nodes, but no change in the liver, spleen or brain. The biochemical findings in mongolism and cretinism have been reviewed by Benda (1947).

(b) *Dietary factors.*—Williams (1949) has discussed the concept of *genetotrophic disease*. According to this view individual human beings possess distinctive metabolic characteristics which are genetically controlled. The well-known “inborn errors” of metabolism may be regarded as extreme cases of partial genetic blocks which are of far wider distribution and which are revealed in the normal variation in the biochemical make-up of the body fluids and tissues. Such genetic blocks may give rise to special individual requirements in the way of specific nutrients, such as amino-acids, vitamins and minerals, in order to compensate for deficiencies. Experimental support for these views was obtained from animal experiments in which rats were given a free choice of diet, when it was found that each individual animal exhibited a distinctive pattern of choice. The individual variation applied also to the consumption of alcohol, which could be varied or even abolished by paying careful attention to the individual needs for other nutrients. It is suggested that these observations may be relevant to the treatment of alcoholism in man. In this connection it may be noted that the synthetic drug, antabuse (tetraethylthiuramdisulphide), appears to act by introducing an artificial metabolic block which prevents the normal oxidation of alcohol to acetic acid. The oxidation is stopped at the acetaldehyde stage, and Larsen, Jacobsen and Hald (1949) have shown that antabuse inhibits the oxidation of acetaldehyde to acetic acid in the perfused liver.

A very outstanding investigation of the effects of prolonged mild dietary deficiencies has recently been completed by a group of workers at the Elgin State Hospital (Horwitt *et al.*, 1948). In this experiment a series of chronic psychotics of various diagnostic types and ages were maintained for no less than three years on a diet mildly deficient in thiamine (0.4 mgm./day) and riboflavine (0.8 mgm./day). A control group received a supplement of yeast, providing a liberal supply of vitamins of the B-group. The investigation was undertaken to ascertain the minimal vitamin requirements of older as compared with younger men, and the influence of low and high intakes of these vitamins on the mental state of psychotics. The results of this experiment indicate that a mild deficiency of thiamine, if sufficiently prolonged, can produce a marked aggrava-

tion of mental abnormalities already present : but the change can be reversed, if taken in time, by giving thiamine. The old subjects, as a group, were more affected than the younger by the mildly restricted diet, and this was true for performance tests stressing speed and manipulative skill as well as for comprehension. Only the older patients developed signs of circulatory insufficiency : neurological signs were also more pronounced and more persistent in the old. The changes in mental state came on very gradually. Most commonly there was a dulling of faculties involving attention, interest, ambition and sociability. This was associated with a decrease in talking and slowing of movement. More severe vitamin restriction precipitated reactions of a more explosive type, such as tantrums, furores and rages. The mild nutritional restriction appeared to reinforce or reawaken potential psychotic trends and patterns already present in the patients.

The biochemical investigation of the paralysis of foxes kept in fox farms led to the unexpected conclusion that it is due to a vitamin B₁ deficiency associated with the eating of raw fish (Green, Carlson and Evans, 1941). It has now been confirmed that the viscera of carp, trout and other fish cause a rapid inactivation of thiamine : as much as 90 per cent. was inactivated in 10 sec. by carp extracts *in vitro*. Extracts of bracken are similarly active in inactivating vitamin B₁, and it is therefore suggested that the similar paralysis syndrome observed in animals after feeding on bracken is also due to thiamine deficiency (Somogyi, 1949). These investigations give evidence that vitamin deficiencies may occur even on diets liberally supplied with vitamins, if vitamin-inactivating principles are ingested at the same time.

Barsky and Hawkins (1948) have described a case of experimental pyridoxin (vitamin B₆) deficiency in a human subject who developed mental confusion and depression, as well as the expected blood changes. The mental symptoms were promptly relieved by administering pyridoxin. Davenport and Davenport (1948) have studied the increased cerebral excitability produced by pyridoxin deficiency in rats. The abnormal excitability, as indicated by the ECT threshold and the occurrence of convulsive seizures, was increased by feeding tryptophane. This was not due to increased formation of xanthurenic acid, which had no effect on the cerebral excitability.

The neurological manifestations of subacute combined degeneration are prevented from progressing, or are improved, in patients treated with microgram doses (40 μ g./week) of the purified anti-pernicious-anaemia factor (Ungley, 1949). The recent isolation of this substance in the pure crystalline state is an outstanding achievement. The substance, now named vitamin B₁₂, is a red crystalline compound containing 4 per cent. of cobalt, and its isolation depended mainly on the use of the new adsorption and chromatographic techniques (Rickes *et al.*, 1948 ; Lester-Smith and Parker, 1948). The relation of the psychic symptoms in pernicious anaemia to the pathological changes in the brain have been discussed by Ferraro *et al.* (1945). Administration of pteroyl glutamic acid (PGA) improves the blood picture and the glossitis but does not affect the neurological symptoms, which may therefore appear more prominent (Wagley, 1948). It would appear, however, that PGA is required for the development of the central nervous system in the young

animal: the occurrence of hydrocephalus in young rats fed on a PGA-deficient diet has been confirmed by O'Dell *et al.* (1948), who showed it could be prevented by addition of PGA to the maternal diet.

(c) *Neurotoxic factors*.—The production of canine hysteria by feeding white flour to the dog was reported by Mellanby (1946). White flour is not a natural product, but is manufactured by the millers by subjecting natural flour to various bleaching processes: treatment with nitrogen trichloride is commonly used as a method of bleaching, and white flour "improved" in this way is known technically as *agenized* flour. Dogs fed on *agenized* flour first develop changes in behaviour: a friendly animal may become irritable and vicious, or an aggressive animal may become quiet. The condition described as canine hysteria then appears: the animals show hyperactivity, which may take the form of uncontrolled running in circles, leading to convulsive seizures. They show EEG changes similar to those seen in epilepsy in man. Biochemical investigation has shown that the effect is due to a toxic substance produced by the action of nitrogen trichloride on the gluten of the flour (Wagner and Elvehjem, 1944). The toxic substance appears closely associated with glutamine in chromatographic separation: it is precipitated from alcoholic solution by mercuric acetate, and work on the isolation of the substance is in active progress (Butler and Mills, 1949; Bentley *et al.*, 1949). Rabbits are also sensitive to the toxic action of *agenized* flour. As used for human consumption, *agenized* flour is usually mixed with flour "improved" by other methods, and no toxic effects have hitherto been reported in man; nevertheless, official steps have been taken, both in the U.S.A. and here, to discontinue its use.

In paralysis due to poisoning by Botulinum toxin the motor nerves appear to conduct normally and the muscles are still excitable by acetylcholine. Torda and Wolff (1947) attributed the failure of neuromuscular transmission to an inhibition of the choline acetylase by the toxin, which exerts a selective action on cholinergic nerve endings (Ambache, 1949). Crude preparations of Botulinum toxin inhibit the choline acetylase of the brain; but Burgen, Dickens and Zatman (1949) have recently obtained purified preparations which do not inhibit the choline acetylase, so that this explanation is no longer tenable. They found that although the nerve fibres were still able to conduct an impulse, the toxin greatly reduced the amount of acetylcholine liberated at the nerve endings. They concluded that the unmyelinated nerve endings are the point of attack of the Botulinum toxin. The toxin is not a lecithinase, but it has been suggested that it might be a hyaluronidase.

Several cases of polyneuritis due to poisoning by orthotricresylphosphate have been reported (Hotston, 1946). This has a selective action on the motor system and picks out the anterior horn cells in particular: the typical signs are foot-drop without sensory changes. The reported cases have generally arisen from the use of orthotricresylphosphate as an adulterant in frying oils, but cases have recently been reported from Germany of polyneuritis due to orthotritolylphosphate incorporated in plastic material used for bags, wrappers and shoes. It is taken up directly by the skin or from food left in contact with the material (Elsaesser, 1948).

It has been shown that *lewisite* and other arsenical poisons have a selective action on the pyruvic oxidase of the brain (Peters, Sinclair and Thompson, 1946). This is one of the enzyme systems containing -SH groups, which are apparently the point of attack. Protection is afforded by 2 : 3-dimercaptopropanol (BAL). The succinic dehydrogenase, which also contains -SH groups, is also inhibited by *lewisite*, but it is less sensitive than the pyruvic oxidase.

Exposure to oxygen pressures of 4 atmospheres or more causes symptoms of *oxygen poisoning* within an hour. The symptoms in man include faintness, fall in the blood pressure and, in some cases, convulsions. Animals may also have convulsions and may develop persistent motor disabilities. Histological examination shows generalized congestion, perivascular oedema, focal areas of necrosis and other degenerative changes in the brain (Bean, 1945). The biochemical aspects of oxygen poisoning have been investigated by several groups of workers (Stadie *et al.*, 1945 ; Dickens, 1946 ; Mann and Quastel, 1946). Tissue from the brains of animals exposed to high oxygen pressures showed a diminished ability to oxidize substrates *in vitro*. It would appear that the respiratory system of the brain is designed to operate at certain optimal oxygen tensions. If the permissible limits of variation are exceeded in either direction the whole system is thrown out of balance, and temporary or permanent damage may be caused.

(d) *Anxiety and depressive states.*—Floger and Jennigs (1946) carried out fractional test meals on 20 students awaiting the results of their M.B. examinations. They found no evidence of abnormality. Schiele and Brocek (1948) describe the production of an "experimental neurosis" in 23 human subjects who volunteered to submit for a period to "semi-starvation" by living on a diet of 1,570 calories per diem. The physical changes included loss of weight, lowered basal metabolic rate, weakness and fall in pulse rate. The psychological effects included intense preoccupation with thoughts of food, emotional changes tending towards irritability and depression, decrease in self-initiated activity, loss of sexual drive and social introversion. Small and Milhorat (1944) found no evidence of any metabolic abnormality in cases of *anorexia nervosa* studied by them. Glynn, Himsworth and Neuberger (1945) noted that *anorexia* is produced by protein deficiency itself, when it depends on deficiencies in particular amino-acids rather than a general deficiency of protein as such. The appetite of rats can be greatly reduced by withholding methionine ; but it is rapidly restored by administration of a minute amount of methionine. Hoefer *et al.* (1946) have contributed a careful study of the mental and physical symptoms in a series of 27 patients suffering from hyperinsulinism (spontaneous hypoglycaemia) with verified islet-cell adenomata of the pancreas. The symptoms complained of included weakness, tremors, confusional states, light-headedness, sweating and headaches. Nausea, vomiting, hunger, pallor, coldness, precordial oppression and palpitations were complained of less frequently. Many of the subjects had fragmentary or complete seizures, and the EEG records showed "convulsive" patterns in most of the subjects.

Greville (1945) has discussed the abnormalities in the glucose tolerance curves commonly reported in anxious and depressed patients. He notes that when the test is repeated at intervals on the same patient the low flat type of

oral glucose tolerance curve may change to the high type at the opposite extreme without significant change in the mental state. Patients with abnormal oral glucose tolerance curves frequently give normal curves when tested by the intravenous method: the abnormality is thus in the rate of glucose absorption and not in the carbohydrate metabolism. This conclusion was confirmed by tests of absorption time by measuring the time taken for potassium iodide taken by mouth to appear in the saliva.

Latner (1947) has confirmed the interesting observation of Macfarlane and Biggs (1946) that the blood of anxious subjects contains an enzyme which causes fibrinolysis, or the breakdown of the clot in a blood sample. Normal individuals do not have this enzyme in the blood and there is no dissolution of the clot in samples kept for several weeks; but in anxious subjects, such as patients about to undergo an operation, the dissolution is complete within three days. The effect could not be obtained in normal rabbits, but it appeared after adrenalectomy. Fantl and Simon (1948) have observed fibrinolysis in blood samples taken from patients after ECT treatment. The effect is apparently due to the release of a plasma protease which is different from trypsin, since it has no action on fibrinogen although it is capable of breaking down fibrin into polypeptides.

Biochemical aspects of neurocirculatory asthenia, or "effort syndrome," have been discussed by Cobb (1947), who observes that the blood lactic acid is often raised in this condition. Success has recently been claimed for the use of lactic acid in the treatment of patients with anxiety and depressive states (Löwenbach and Greenhill, 1947). The mechanism of this action is not known, but the view that it acts by raising the glycogen level in the liver would appear a possible explanation. Biochemical aspects of anxiety were reviewed by Richter (1945 and 1949).

(e) *Epilepsy*.—Elliott and Penfield (1948) examined biopsy specimens of human focal epileptogenic cortex, but found they did not differ from the normal in their rate of oxygen uptake, carbon dioxide evolution or glycolysis. Pope *et al.* (1947) found normal indophenol oxidase activity, but reported a significantly increased acetylcholine esterase activity in epileptogenic areas from human subjects and also in cortical areas from monkeys rendered epileptogenic by the application of alumina cream. The increase in acetylcholine esterase activity in these experiments was about 40 per cent. above that of normal cerebral cortex. They conclude that "therefore, an increased potential turnover of acetylcholine accompanies the abnormally intensified neuronal activity in cortical areas that are the source of focal epilepsy." The method of producing focal epileptogenic lesions in the monkey by the application of sterile alumina cream to the motor cortex (Kopeloff *et al.*, 1942) is likely to prove useful for experimental work. A high proportion of monkeys treated by this method develop, within three months, spontaneous, recurring, Jacksonian attacks indistinguishable from such attacks occurring in man. E.E.G. studies showed the occurrence of abnormal patterns characterized by delta activity, spike discharges, and "sharp formations" in the region of application of the alumina cream, and demonstrable prior to the onset of clinical seizures. There was also evidence of the progressive development of a secondary mirror focus

in the opposite hemisphere. The seizures could be controlled by the use of phenobarbitone or epanutin.

It has been reported that appreciable amounts of acetylcholine may be found in the CSF and that the amount is abnormally high in epileptics (Coloma, 1943; Tower and McEachern, 1949). The biochemical changes associated with convulsive activity were discussed in an earlier section. Other biochemical work has been summarized in a recent Symposium on Epilepsy (Lennox, Merritt and Bamford, 1947).

(f) *Psychoses*.—Studies on brain biopsy specimens from the temporal lobes of cases of Pick's Disease and Alzheimer's Disease have shown that, besides the marked chromatolysis and other histologically recognizable degenerative changes, there is a reduction in the indophenol oxidase and peroxidase reactions and an increase in the acid and alkaline phosphatases (Polatin *et al.*, 1948). The brain lipids were found to be within normal limits in one case of Alzheimer's Disease; but there was depletion of phospholipids in the grey and white matter, and an increase in the phosphorus content of the non-extractable residue, consisting mainly of glial tissue, in cases of senile psychosis, disseminated sclerosis and vascular syphilis (Weil, 1948).

Considerable interest attaches to the studies of Winifred Ashby and her collaborators on the distribution of the enzyme carbonic anhydrase in the different cytoarchitectonic regions of the brain. This enzyme, which catalyzes the reversible reaction between carbon dioxide and water to form carbonic acid, is believed to be concerned in the maintenance of the normal pH of the tissue. Normal individuals show a relatively high concentration of the enzyme at the occipital pole and a low level in the temporal area. Brains from patients with organic psychoses associated with arteriosclerosis or with general paresis showed a patchy asymmetry of the enzyme content in the two hemispheres of the brain. Deteriorated schizophrenics showed an abnormally uniform distribution of the enzyme over the whole cerebral cortex and a lowering of the enzyme content in areas which are active in the normal brain. She concludes that a metabolic disturbance associated with imbalance in the quantitative relations of essential enzymes may be the cause of the mental dysfunction (Ashby, 1947; Ashby and Weickhardt, 1947).

Klein and Nunn (1945) have reported the biochemical findings in a case of manic-depressive psychosis showing regular weekly cycles. There was a rise in the blood pressure, pulse rate and respiration rate in the manic phase, with a fall in the depressive phase. The basal metabolic rate was +30 in the manic, and -10 in the depressive phase. There was a retention of salt and water, with a gain of 2-3 lb. in weight in the depressive phase and a release in the manic. Lindsay (1948) has also observed rhythmic changes in the body weight of two periodic catatonics studied over a long period. Exacerbation of the symptoms was associated with a loss of weight and remission with a gain. He regards the phasic mental changes as not causally related to the metabolic changes: both are indications of a dysfunction of the central nervous system, probably hypothalamic in origin.

Recent work has given ample confirmation of the well-established unresponsiveness of the chronic schizophrenic to stimuli of many kinds, and

numerous experiments are described by Hoskins (1946) which agree with this conclusion. Pincus *et al.* (1949) studied the lymphocytopenic response and the excretion of 17-ketosteroids following exposure to stresses such as heat and cold. The normal responses failed in a high proportion of schizophrenics, who showed, however, a normal response to the administration of active corticosteroids. Administration of adrenocorticotrophic hormone failed to produce a normal response in the schizophrenics, and this gave evidence that their adrenal cortical function is impaired. It may be noted that the response to other stimuli, such as glucose administration, was absent in only a smaller proportion of the schizophrenics, and Parsons *et al.* (1949), who studied the response to adrenaline administration, found no significant difference in the lymphocytopenic or hyperglycaemic responses of schizophrenics and normal controls. The schizophrenics differed from the normal subjects, however, in showing far less response to emotional stress. They conclude that the pituitary-adrenal relationship is not necessarily impaired in schizophrenics, but there is a constant defect in the communications between the higher centres and the endocrine system. The nervous pathway responsible for the lymphocytopenic response to emotional stress has recently been investigated in the rabbit by de Groot and Harris (1950). The normal response could be elicited by stimulation of the posterior region of the tuber cinereum or of the mammillary body in the unanaesthetized animal. Stimulation of a number of other regions in the hypothalamus or pituitary gland did not give it. The response was abolished by lesions made in the zona tuberalis, but not by lesions interrupting the infundibular stem. They conclude that the secretion of adrenocorticotrophic hormone, which is responsible for the lymphocytopenia, is controlled by the hypothalamus by a humoral mechanism conveyed via the portal vessels of the pituitary stalk. This may be an adrenergic mechanism mediated by the release of a sympathomimetic substance into the portal vessels by the hypothalamus.

Greville (1945) has collected the results of a number of investigations by the hippuric acid excretion method on the liver function in schizophrenics. The figures give little support for a specific impairment of liver function in catatonic schizophrenics, but they indicate that impairment of liver function is fairly common in schizophrenics as a group. Koersner (1947), and Georgi *et al.* (1948) have both been able to confirm the occurrence of liver dysfunction, as shown by this test, in a variable proportion of schizophrenics, and the latter workers report that the impairment is more marked in the early acute cases than in the longstanding chronic cases. By using a modified test, in which they administer benzoic acid and glycine together, they have been able to show further that the failure is due to an impairment of the ability to mobilize glycine, i.e. the defect is apparently in the nitrogen metabolism and not in the enzyme system which couples glycine with benzoic acid. They conclude that the liver dysfunction in schizophrenia may be secondary to a general toxicosis and, in support of this thesis, Georgi, Fischer and Weber (1949) have shown that there is a similar impairment of liver function in mescaline intoxication.

A number of investigators have reported the experimental production of pseudo-schizophrenic states by the administration of different toxic substances and drugs. Kandors (1949) describes the production of psychotic symptoms

of schizoid pattern in normal subjects given extremely small doses of 20–40 μ g. of lysergic acid, a new derivative of ergotamine. Hernandez and Dalman (1948) describe the production of psychotic symptoms presenting a schizophrenic picture in two subjects of schizoid personality by acute intoxication with an overdose of amphetamine. Abnormal behaviour, characterized by the production of stereotyped postures, may also be induced by amphetamine in experimental animals (Chance, 1947). Psychoses following the administration of atabrine for the treatment of malaria have been widely reported: the incidence was as high as 0.1 per cent. of all cases treated. The form of the psychosis depends on the previous personality of the patient and manic reactions tend to predominate, but reactions of schizophrenic type occur in about 30 per cent. of those affected (Perk, 1947; Griebner, 1947).

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ELECTRO-ENCEPHALOGRAPHY.

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SINCE the appearance of the last volume in this series, the practical and theoretical advances in electro-encephalography have been so great that the subject should be considered for promotion from a technique to a science. Recognition of this up-grading is delayed partly because no self-respecting worker would relish being called an electro-encephalologist, but the development is implicit in the designation chosen for many new departments as "electro-physiological." Following the example of the British group of workers, several E.E.G. societies have been formed in other countries. An international congress was held in 1947 (International E.E.G. Meeting, 1947), and a second one in 1949 in Paris. A special international Journal has appeared; this may help to concentrate publications in this field, which hitherto have been spread over scores of journals in many countries.

As a consequence of the rapid expansion of interest and activity the number of papers with psychiatric interest or implications during the last five years is far too large to be dealt with completely. Several reviews and works of general interest are available (Adrian, 1947; Cobb (S.), 1948; Darrow, 1947; Delay and Verdeaux, 1946-7; Frey, 1946; Gibbs, 1945, 1946*a, b*, 1947; Hoagland, 1947; van der Horst, 1947; Jasper, 1947; Jasper and Kershman, 1946; Lennox and Lennox, 1947; Liberson, 1948; Remy, 1945, 1947; Walter, 1946; Walter and Walter, 1949*b*).

The first book on electro-encephalography dealing with every aspect of the subject by several authors under the editorship of Hill (1950) has appeared.

TECHNIQUE.

Apart from the multiplication of centres, which does not in itself signify progress except in the rate of production of apparatus, there has been a real advance in the attitude of many E.E.G. investigators; who are tending more and more to study the electrical activity of the brain in conjunction with other variables, and under the influence of controlled stimuli. Only in the most overworked and understaffed centres are records taken in passive or uncontrolled conditions. It is from such dynamic experimental procedures that the most promising results have been obtained; inevitably they depend upon careful teamwork and intricate equipment. A modern electrophysiological department contains more electronic gear than would have been found in all the combined E.E.G. laboratories in the world ten years ago. The technical devices responsible for most active progress are:

1. The general adoption of multi-channel amplifiers and recorders. The most modest centre has a four-channel instrument; several employ a number of

six- or eight-channel machines with a correspondingly large staff of recordists, engineers and interpreters.

3. Automatic methods of analysis. Three new types of analyser have been invented (Baldock and Walter, 1946; Barbour, 1947; Hoefer, Markey and Schoenfeld, 1949).

4. The reintroduction of the cathode-ray tube with complex display systems to extend the scope of spatial, temporal and frequency analysis, as an adjunct to the conventional voltage-time records (Bates, 1949; Kibbler and Richter, 1949; Walter, 1947).

5. The provision of controlled stimuli, particularly of the rhythmic photic and auditory type (Dawson, 1947*a* and *b*; Gastaut, Roger and Gastaut, 1948; Shipton, 1949; Walter, 1946, 1949; Walter and Dovey, 1947; Walter, Dovey and Shipton, 1946; Walter and Walter, 1949; Walter, Walter, Gastaut and Gastaut, 1948).

6. The application of biochemical techniques to control and measure changes in the internal environment (Hill, St. John Loe, Theobald and Waddell, 1948).

7. The employment of a variety of transducers and display systems to register physiological variables such as pulse rate, respiration, skin resistance, movements and the like (Darrow *et al*, 1945, 1946, 1947; Hill *et al*, 1948).

8. The exploration of the more inaccessible parts of the central nervous system with special types of electrode (Gastaut, 1948; Gastaut, 1949; Lennox and Ruch, 1946; Roubicek and Hill, 1948; Walter and Dovey, 1946).

In some experiments all seven of these technical stratagems are employed together; in many three or four, with the result that attention need no longer be concentrated on the gross aberrations familiar in epilepsy and organic disease. The central nervous system is coming to be considered as an elaborate device for handling signals; slight variations in the way in which the signals are transmitted, transformed and displayed are found to be valuable clues to the nature and extent not only of normal processes, but also of mental and organic disorders. Consideration of neurophysiological problems in this fashion is sometimes regarded as a separate discipline under the title of "Cybernetics" (Wiener, 1948; Ashby, 1949, and chapter by Ashby in this volume, Walter, 1950).

The high resolving power of modern equipment, the development of experimental procedures and the effort to think of central nervous function as a whole, have together broken down the sharp but arbitrary divisions between "normal" and "abnormal" criteria. These were based on the empirical correlation between well-defined neurological disorders and such obvious features as the wave-and-spike pattern of *petit mal* and the delta activity of acute cerebral lesions. The correlations remain and in routine clinical electroencephalography they are of undiminished value as aids to diagnosis, but as predicted in an earlier review (Walter, 1944), the subclassification of abnormal records by means of quantitative analyses has promoted both more detailed clinical interpretation and a better understanding of the relations between grossly abnormal phenomena, the similar features from certain normal individuals and the more elusive components of arbitrarily normal records. "The

main feature of brain function is the enormous adaptability of its components. . . . Each element of the brain seems capable of a multitude of activities. Study of the number and interrelation of these activities is the basic problem of neurophysiology, and electro-encephalography is of unique importance only in so far as it contributes to that study."

For the purposes of this review, progress will be considered mainly in so far as it aids understanding of the relation between the various electrical modes of cerebral activity and the varieties of physiological or pathological function.

CLASSIFICATION OF ELECTRICAL FEATURES.

The electrical activity of the brain might be considered under two main headings—Spontaneous and Evoked. In the first category would be the components which "are not obviously caused by changes occurring at the time of the experiment." But this classification is a utilitarian, not a fundamental one, for it is based not on the nature of the brain, but on the intentions of the experimenter. The essential and perpetual function of the brain is to model and to mould the environment; the experimenter may attempt to limit or control these functions, but he must realize that his efforts can never be wholly successful. It would be mere sophistry to argue whether the augmentation of an alpha rhythm after a subject has been told to close his eyes is an evoked or spontaneous effect; "it is difficult to prove in the case of an organ so specialized for storage and memory as the brain, that apparently spontaneous activity is not the indefinitely prolonged after-effect of some previous experience." None the less, it is useful to distinguish between activity appearing when the subject is functionally at rest, and that which immediately follows the application of controlled stimuli.

Classification of activity according to frequency and waveform is of even less value since a rhythm which is normal in one region and in certain conditions may in other conditions and other areas be associated with a profound pathology. Here again it is useful to have brief designations for the various forms of rhythmic and paroxysmal discharges, but these designations are used with some connotation of provenance and significance as well as of frequency and form.

Perhaps it is not surprising that information about the brain is too multi-dimensional to be tabulated on paper; however, an attempt will be made by combining electrical and functional data to outline the shadow of a pattern.

Delta rhythms.—This term was coined for the slow electrical rhythms associated with acute cerebral lesions, but has been used by some workers to describe any activity below 8 c/s, while others have referred to rhythms at 5–7 c/s as slow alpha rhythms. Both usages are confusing: the term delta is now reserved for activity at frequencies below 4 c/s when associated with signs of cortical dystrophy or dysfunction. In 1944 (Walter and Dovey) components between 4 and 7 c/s were identified as separate phenomena and given the name theta rhythm.

An important feature of delta activity is that it can appear in any part of the brain, either in association with a lesion, in deep sleep or in infancy. It is usually possible to show that cortical function is depressed or absent in the presence of delta activity, whatever may be its immediate cause, and in

general the lower the frequency the more profound the depression. It has been suggested (Walter, 1948) that synchronized electrical oscillation of this type may have some sort of protective function when the normal activity of the cortex is disturbed. There is no doubt that the passage of very low frequency electric currents through the brain has a sedative or narcotic effect, producing in normal subjects a feeling of drowsiness and lethargy without stimulation. If delta activity were an unimportant result of cerebral distress, it is difficult to see why the causal relationship should be reversible. It is still not clear, however, what neural mechanisms are involved in these rhythms. When they occur close to a cortical lesion they are usually unaffected by external stimuli, but when, as is occasionally the case, they arise in more distant regions or in the homologous area of the opposite hemisphere, the delta discharge is more rhythmic and often reduced by an increase in alertness on the part of the subject, in this way resembling some of the normal alpha rhythms. It would appear, therefore, that delta activity can be produced both by interference with the superficial cortical circuits and in normal cortex by "driving" through anatomical pathways, in which conditions the delta driving process and normal physiological stimuli compete for government of the area concerned. The delta rhythms seen in normal adults during hypoglycaemia, alkalosis, anoxia, deep anaesthesia and sleep are so diffuse, symmetrical and often so large that implication of cortico-basal circuits is almost certain. In animals similar slow discharges in all areas of the cortex can be produced only by stimulation of midline thalamic nuclei at a frequency of about 3 per sec. (Drooglever-Fortuyn and Jasper, 1947). Photic stimulation at frequencies below 4 f/s rarely evokes a large cortical response except in children between the ages of 6 and 12 years, but stimulation at higher frequencies evokes slow activity in some normal and many epileptic subjects. In normals the appearance of such a response is associated with feelings of confusion and disorientation; in epileptics with more profound disturbances of consciousness. Clinical seizures do not occur unless there is a faster component with the slow discharge; when this appears the electrical and clinical signs of *petit mal*, *grand mal* or myoclonic epilepsy are an invariable accompaniment. In both normal and clinical subjects a slow rhythm evoked by photic stimulation bears a numerical relation to the stimulus frequency and the resonance is often quite sharp, suggesting that well-defined retroactive circuits are being excited.

Darrow and his associates (1945, 1946, 1947) have suggested that the ease with which slow activity can be evoked by overbreathing depends in some way upon the level and balance of autonomic activity, reduction in the para-sympathetic tone being accompanied by increased slow activity.

The pressure of organic evolution and the compactness of central nervous organization leave little room for phenomena without significance, and it would be surprising if the opportunities for widespread feed-back networks offered by cerebral anatomy were not employed to provide a mechanism for "failure to safety." Such a device is essential for any artificial complex machinery; its absence in the brain would permit every slight local disturbance to involve every other region in a perpetual series of functionless and destructive discharges—epilepsy would be the rule rather than the exception.

Theta rhythms.—This term was introduced to distinguish components at 4–7 c/s from those of delta frequency in records from patients with subcortical tumours. The correlation of this type of activity with lesions in the regions of the thalamus and third ventricle has been confirmed by Cobb (1944, 1945) and Laufer (1947). Theta activity is the principal component in records from normal children between 2 and 6 years of age, in some of these it is often responsive to emotional stimulation, and occasionally several components within this band can be identified by their differential response to pleasant and unpleasant stimuli. Hill (1944) has described similar theta rhythms in aggressive psychopaths, and this feature is common in certain types of violent criminal (Hodge, 1945). Even in some apparently normal adults theta activity can be detected, particularly with automatic analysis, and it is usually possible to find some stimulus or association which augments this theta component, sometimes with coincident signs of autonomic disturbance.

If theta activity is a sign of disturbance in the cortico-thalamic and basal circuits, one would expect to find these rhythms in records taken with pharyngeal electrodes from patients with known lesions of the basal structures. This was confirmed by Roubicek and Hill (1948), who found a moderate potential theta discharge from the region of the pharynx in cases with pituitary tumours, even when no such activity was visible in the scalp leads. The effect was particularly marked when closely spaced bipolar electrodes were used in the pharynx, a system preferred also by Gastaut (1948). With bipolar leads very high amplification must be used, and the incidence of artefacts is more troublesome, but the improved accuracy of location justifies the additional trouble.

There is, of course, no reason why a mere similarity of frequency should be considered evidence of identical significance, but in all conditions, normal and pathological, in which theta activity appears in the parieto-temporal region there is evidence of some disturbance or immaturity of the cortico-thalamic relations or of autonomic instability. As in the case of the delta rhythms, photic stimulation provides confirmatory evidence. At stimulus frequencies of about 6–7 f/s some normal subjects exhibit an unusually large response, not from the visual, but from the more anterior regions. This is associated with peculiar sensations often of a kinaesthetic or abstract type with considerable affective accompaniments. Both the electrical response and the subjective sensations can be augmented if the subject abandons himself to the sway of his feelings, and attenuated if he deliberately assumes a cool and rationalistic attitude. Adults who show these effects usually have a significant amount of theta activity in their resting records and some signs of ingenuousness, provocative candour or repressed aggression in their personalities. The theta components in young children, however, are not usually susceptible to photic augmentation, but are most sensitive to primitive emotional stimulation. Experienced adult subjects can predict the probability of an exaggerated evoked response in the theta band by introspective assessment of their mood, bad temper going with a large response; they can also detect the appearance of such a response by the transitory exacerbation of their irascibility. It is possible that the archaic meaning of "temper" may have a modern quantitative revival.

In adult subjects, apart from photic stimulation, only very offensive positive stimuli evoke theta activity, but *withdrawal* of an *agreeable* stimulus is often effective (Walter, 1950). In such conditions the theta rhythm grows slowly over a period of about ten seconds after the pleasant sensation has ceased and then usually ceases suddenly. The detailed pattern of the record during this period is sometimes remarkably constant from experiment to experiment, suggesting that a stereotyped attitude or feeling of frustration is being displayed electrically; introspection confirms this to some extent, and since a similar but less specific feeling can be evoked by rhythmic photic stimulation, with electrical responses at the same frequency, and in the same area, but with different fine-structure, the possibility of demonstrating a direct functional linkage between mental and electrical events seems worth considering.

From the statistical standpoint, Rey, Pond and Evans (1949) have reported significant correlations between temporal activity in the theta band and laterality, sex of the subject, and irritability of personality, as well as with epileptoid manifestations of various sorts.

In neurologically normal persons theta activity can be evoked by:

1. Extremely unpleasant emotional stimuli.
2. Withdrawal of pleasant stimuli.
3. Rhythmic photic stimuli within the theta band.
4. Frequency modulation of photic stimuli so that the difference between upper and lower frequencies is within the theta band.
5. Stimulation at multiples of a theta frequency.
6. Stimulation with two sources at frequencies whose difference is within the theta band.

All these methods including spontaneous changes, emotional stimuli and photic activation are additive and reversible, suggesting that they form a congruent set.

In epilepsy and allied conditions theta components are often prominent between seizures, but are not always recognizable without analysis since the ratio between theta and alpha frequencies is a particularly difficult one for the eye to deal with (Dawson and Walter, 1944). Furthermore the triangular, saw-toothed, flat-topped, monophasic and sharp waves which are found in so many patients with epileptoid disturbances (Goodwin, 1947; Waggoner and Bagchi, 1946), are all the resultant of delta and theta components with various phase relations, and these components can be separated by careful location studies. The relation between epilepsy and subcortical disturbances is clarified by the observations of Lennox and Brody (1946), that out of 211 patients with "psychomotor" waves only 135 were epileptic, while 31 had signs of subcortical lesions. It is interesting to note that, whether epileptic or not, the symptoms of patients with such records are often relieved by anti-convulsant therapy, e.g. hydantoinate (Walker and Kirkpatrick, 1947). It should be recalled also that the appearance of activity at 6-7 c/s is the commonest prelude to an epileptic seizure, whether major or minor, and whether spontaneous or induced by drugs or by electrical or photic stimulation.

Alpha rhythms.—Until a few years ago it was usual to speak of "the alpha rhythm," and some indeed used the term as almost synonymous with E.E.G. Familiarity bred, if not contempt, at least a remarkable indifference or lack of curiosity about the function of this activity. Recently, however, it has

been shown that nearly always the alpha rhythm is complex (Dubouloz, Gastaut and Corriol, 1948; Cohn, 1948; Walter, 1947; Walter, in Hill, 1950). Usually there are several components present at the same time in the 8-13 c/s band, and often harmonics at 16-30 c/s. These components may be distinguished by analysis, by their differential response to mental and physical stimuli, and by spatial separation. Several hypotheses have been put forward as to their function, the most elaborate and suggestive being that they represent the output of group-scanning generators transforming the spatially displayed projection of visual images into a cipher on a time base. (McCulloch, 1947; Pitts and McCulloch, 1947; Walter, 1947; Walter and Walter, 1949*a* and *b*; Wiener, 1948). This hypothesis has the advantage that at least it defines a worthy role for the central nervous structures and demands electrical synchronization instead of dismissing it as a convenient accident. The presence of several alpha rhythms suggests the possibility that, in such mental processes as recognition, recall and imagination, a succession of real, remembered and invented scenes can be anatomically superimposed and compared. This concept helps to explain the differences between individuals and the relation of these differences to habits of visual imagery (Golla, Hutton and Walter, 1943).

Subjective effects during photic stimulation within the alpha band of frequencies support the notion of the alpha rhythms as space-time transformers, for the temporal succession of stimuli gives the illusion of a spatial pattern. Since stimulation of this sort with white lights also gives rise to illusions of colour at certain frequencies, it may be that some of the alpha rhythms are associated with colour discrimination. The electrical responses to photic stimulation within the alpha band are complex and vary according to the features of the resting alpha rhythms (Walter and Walter, 1949*a*). One of the more interesting characteristics is that in most people the evoked response as well as the alpha activity is diminished in amplitude, and the harmonic content is increased, when the subject makes an effort of imagination.

A similar effect appears to be produced by some organic lesions of the visual pathways. It is conceivable that in both visual imagination and organic disturbance fundamental components of the visual afferents are diverted from the secondary visual cortex, which then receives a larger proportion of selected harmonics from other sources.

Darrow (1946, 1947) takes a somewhat different view of alpha activity, suggesting that it may be a determinant of cortical repose. On this hypothesis rhythmic activity with the properties of the alpha rhythm acts as an escape-ment, which releases cortical energy during each half cycle; it is even suggested that alpha activity may be a cause of cerebral vaso-constriction by reducing the local metabolic rate.

A time-correlation between some component of the alpha rhythms and voluntary motor activity has been established by Bates (1949) and by Kibbler and Richter (1949). Bates used the method of linear superimposition on records obtained when a subject was asked to make some movement whenever he felt like it. The action potentials from the muscles voluntarily innervated were used as the fiduciary mark for superimposition, and it was found that for

about one second before the "random spontaneous voluntary" movement the sequence of alpha waves followed a stereotyped pattern, and the movement occurred always at about the same phase of the alpha rhythm. This suggests that a signal from one end of the alpha circuits may be used as a "gate" to release voluntary motor impulses only at certain moments determined by the state of sensory integration. The value of such a device in artificial servo systems is well known and its incorporation in the brain is perhaps to be expected, certainly to be admired.

As a corollary of these more detailed theories of alpha activity, rhythms in the 8-13 c/s band in non-visual areas should not at the moment be considered as alpha rhythms. If it can be demonstrated that rhythms with similar functions are a part of central nervous function in other sensory and effector modes, it may be legitimate and desirable to broaden the application of "alpha" to include them or to group them with the visual alpha rhythms under some other designation. Frequency alone should not be regarded as a diagnostic feature.

In psychiatric disorders characterized by transient motor confusional episodes, rhythms at about 10 c/s have been observed in the frontal regions (Hodge, 1945). These are not affected by sensory stimulation and fluctuate independently in the two hemispheres. Kennedy, Gottsdanker, Armington and Gray (1948) have described a rhythm at 8-12 c/s in the fronto-temporal region of some normal subjects which was augmented during mental activity. They suggest this should be called "kappa" rhythm and claim that when this feature intrudes when the subject is trying not to think, it corresponds to momentary thoughts. The occasional appearance of rhythms at 8-13 c/s in non-visual regions would be expected on the scanning hypothesis as a side-effect of the transmission from one region to another of integrated signals. Such activity might be similar in frequency to a component of an alpha rhythm blocked in the occipital region, not by opening the eyes, but by mental activity.

Frequencies above 13 c/s.—Components above the alpha band are seen in all records, but since they do not form a homogeneous group and their relation to function is still in doubt, no simple designation can yet be suggested, although some authors refer to them without qualification as "beta" rhythms. As mentioned above, many of these components are harmonically related to the alpha rhythms and the alpha harmonic content of a record is often found to vary with the level of stimulation and degree of alertness, sometimes inversely with the alpha rhythm itself. This effect is particularly prominent during photic stimulation, and, as already remarked, there seems a possibility that certain forms of information are conveyed by modulation of the harmonics of the scanning rhythms. An important clue may be that in epileptics, rhythmic sensory stimulation in the band which includes the second harmonics of the alpha rhythms, is particularly effective in evoking electrical and clinical seizures, though the fundamental frequency of the seizures pattern may be the fourth or fifth subharmonic of the stimulus frequency.

The significance of activity in the higher frequency bands is always difficult to assess, since muscle action potentials mimic the brain discharges very closely; discrimination is particularly difficult in psychiatric cases where

muscular tonus and voluntary tension are exaggerated or fluctuating. Cohn (1946) and Shpilberg (1947) have observed that activity at 14-30 c/s is common in conditions of mental tension whether normal or psychoneurotic. This has been observed by nearly all E.E.G. workers from time to time, and it is quite usual for normal subjects, particularly females between 14 and 20 years old, to exhibit considerable activity at these frequencies during which time they show other signs of anxiety and apprehension; the electrical and psychological anomalies subside, together with reassurance and accommodation. In some psycho-neurotic and psychotic subjects the presence of components at 14-25 c/s together with the alpha and theta rhythms gives the record a characteristic appearance originally described by Davis (1942) as "choppy." It is interesting to note that in certain normal subjects photic stimulation at these frequencies evokes a complex discharge in the fronto-temporo-parietal region lasting only for a few seconds, but accompanied by disagreeable sensations which if persistent would be regarded as psychotic. As already mentioned, the electrical and subjective effects can be reinforced or attenuated by spontaneous or voluntary mood changes. In patients in whom tension is combined with latent aggressiveness the high frequency activity is usually prominent at first, theta components being minimal. As the patient becomes more placid superficially—often after several records have been taken—the high frequency components subside and a prominent theta rhythm appears intermittently. At this stage the aggressive component usually becomes manifest and may be susceptible to psychotherapeutic management.

Goodwin (1947) and Proctor (1947) found that many psychiatric patients with such various symptoms as headache, emotional or vaso-motor lability, and disturbance of consciousness and personality, exhibited activity in the band of alpha harmonics. The most successful medication in such cases was hydantoinate, whether or not the patients complained of epileptoid disturbances, while barbiturate drugs were of little value except in combination with hydantoinate in the cases with overt convulsions.

Spikes.—In resting records brief discharges with this designation are found only in pathological conditions, usually associated with seizures. They are nearly always strictly focal and their location is often of great value to the neurosurgeon. Transients of this type probably correspond more closely to cortical action potentials than do the various forms of rhythmic activity. When surface electro-positive they are taken to indicate the arrival of afferent volleys, when negative the discharge of cortico-fugal impulses. It is not uncommon for a primary focus of spikes to have a mirror focus in the opposite hemisphere, particularly when the temporal lobe is involved; this region seems to be the site of election for spikes in epileptics with a history of birth trauma.

Although records from normal subjects taken with the usual amplification do not show isolated spikes in the usual sense, analysis reveals the presence of many components in the higher frequency bands and careful examination of the records shows that there is considerable activity with the time-relations of abnormal spikes, but their distribution in space and time is so random that they are easily overlooked. The fundamental anomaly in pathological records of this type is not the waveform or brevity of the discharge, but its mag-

nitude, which is due to the synchronization of numerous cortical units over a relatively large area.

It should be remembered that the elementary electrical response of the cortex to sensory stimulation is in the nature of a spike followed by several slower waves. This can be seen when a sensory nerve is stimulated electrically and records are taken with high amplification from the sensory-projection area (Dawson, 1947*a* and *b*), and during photic stimulation from the occipital lobes in some subjects. The response is visible in such conditions because the stimulus sets up a synchronized volley of impulses, whereas in normal circumstances the cortical activity is as irregular and heterogeneous as the details of the sensory fields. In some normal subjects and many epileptics, hypersynchrony induced by rhythmic sensory stimulation leads to the discharge of spikes in the frontal regions, and this is usually associated with muscular jerks which can evolve into a major convulsion (Dawson, 1947*b*; Walter and Walter, 1949*a*). In such cases the subjective sensations are usually much less marked than when the stimulation augments the resting rhythms, in spite of the more dramatic motor manifestations.

Wave and spike.—This pattern, is of course, generally regarded as diagnostic of epilepsy, in the sense that it is an invariable accompaniment of *petit mal* seizures and, when it occurs in patients who have never complained of such attacks, can be shown to be associated with a disturbance of consciousness. The extremely high voltage of this discharge is as significant as its waveform, for it indicates the involvement of very large groups of cortical neurones. It is remarkable that despite the great amplitude of the discharge and the presence of a sharp spike, motor accompaniments are absent or minimal during a *petit mal* seizure. Since a discharge of spikes without waves at this amplitude is nearly always associated with muscular jerks or jactitation, it seems possible that the transmission of impulses to the periphery may actually be prevented in some way by the slow component of the wave and spike pattern. This suggestion should be considered as a corollary to the proposition outlined above, that delta activity may have a protective function.

The wave and spike formation can be synthesized from a number of pure sine waves (Dawson and Walter, 1944). It does not necessarily follow that natural wave and spike is generated in this way, but analysis of inter-seizure records from epileptics usually discloses many components with quasi-harmonic relations, and immediately before a seizure it is often possible to observe the augmentation of one or more of these components and their confluence into the characteristic discharge (Walter, 1946). Spatial analysis of wave and spike rhythms permits separation of many components, and on the basis of these observations it is suggested that, in some cases at any rate, the minor seizure pattern is produced by synchronization of pre-existing rhythmic components previously just out of step. This hypothesis is supported by the discovery that wave and spike discharges can be evoked in some epileptic patients by rhythmic physiological stimulation at the frequency of one of the resting components (Walter, Dovey and Shipton, 1946). Extensive studies (Gastaut, Roger and Gastaut, 1948) have confirmed this observation, and after attention was directed to the efficacy of photic stimulation, several clinical cases have been

reported (Cobb, 1947) in which accidental exposure to flickering light had induced a seizure. Understanding of the mechanism of this effect is assisted by the experiments of Drooglever-Fortuyn and Jasper (1947), who found that electrical stimulation at about 3 c/s of the dorso-medial nucleus in cats could evoke generalized wave and spike discharges in the cortex. Detailed study of human material has produced evidence that the generation of wave and spike by photic stimulation is due to interaction between visual afferents and spontaneous cortico-thalamic rhythms at the thalamic level. The increased proportion of wave and spike during sleep, reported by Gibbs and Gibbs (1947), and the action of other activating agents such as hyperpnoea, metrazol, hypoglycaemia (Baisset *et al*, 1948; Cure, Rasmussen and Jasper, 1948; Kaufman, Marshall and Walker, 1947; Ziskind, Sjaardema and Bercl, 1946) may be attributable also to augmentation of some component of the resting rhythms.

As in the case of spikes, it is the hypersynchrony which seems the fundamental anomaly in seizure discharges, and attention should be directed to discovering the reasons for this feature in the various types of epileptics. The remarkable ease with which seizures can be induced by photic stimulation in cases of familial myoclonic epilepsy (Fairweather, O'Sullivan and Walter, 1948; Walter and Walter, 1949*a*) suggests that one cause at least is a genetic disturbance. It seems likely that similar electrical and clinical effects can be produced by a variety of disturbances affecting the frequency and distribution of activity in cortico-thalamic retroactive circuits; clinical seizures are frequent only in individuals in whom several of these disturbing factors are present at the same time.

The wide variety of anticonvulsant drugs and the irregularity of their action can be more easily understood on the basis of these hypotheses, since any agency which can alter even slightly the frequency, phase relations or anatomical distribution of any of the resting rhythms may reduce the likelihood of a seizure pattern developing, although the efficacy of such treatment would depend upon the detailed physiopathology in each case.

APPLICATIONS TO NEUROPSYCHIATRY.

From the diagnostic standpoint, routine passive electro-encephalography is of limited value to the psychiatrist. It can help to distinguish between truly epileptic disturbance and psychopathic impulsive and compulsive behaviour; but in many psychopathic and behaviour disorders, distinct abnormalities have been found, usually of the theta type, and these are not always easy to distinguish from the epileptic patterns. The features of such records have been described by many workers (Gottlieb, Ashby and Knott, 1946, 1947; Hill, 1944; Hodge, 1945; Kibbe, 1947; Mosovich, 1946; Rockwell and Simons, 1947; Simons and Diethelm, 1946; Simon, O'Leary and Ryan, 1946; Taylor and Pacella, 1948; Walker and Kirkpatrick, 1947), but their interpretation is still a matter for debate. The uncertainty is not entirely the fault of the electro-encephalographer since there is often great variation between centres in the significance attached to the various psychiatric labels, and furthermore, the mental state of the patient at the time of the examination is an important factor which is often impossible to assess even in qualitative terms.

As in the case of epilepsy, it is sometimes more satisfactory to control the stimulus levels, since even in mental disorders, slight anomalies may then be exaggerated; on the other hand, interesting features often appear at some stage of somnolence. Diaz-Guerrero, Gottlieb and Knott (1946) found that in six patients with depressive psychosis, there were more frequent transitions from one level of sleep to another as indicated by the changes in the E.E.G., and there was also a preponderance of light sleep as compared with normal subjects. Liberson (1947) has also described interesting variations in the E.E.G. patterns during sleep in various types of mental disturbance. Though more variable than was at first believed, sleep patterns are sufficiently definite to prove an objective method of distinguishing true sleep from hypnotic trances, hysterical states and stupors (Dynes, 1947). Recording during induced insulin shock treatments is helpful in following the development of coma and avoiding complications.

The establishment of norms for children and adolescents of all ages (Henry, 1944; Walter *in* Hill, 1950) has helped to scale the anomalies frequently found in children with behaviour disorders, but Eickoff and Beevers (1947) could not distinguish between records from normal and disturbed children. As an aid to the planning of treatment, electro-encephalography seems to be of some assistance, since patients with even slightly abnormal records appear most likely to benefit from anticonvulsant drugs more than do those with normal records. (Walker and Kirkpatrick, 1947). Hill (1947) found that in aggressive psychopaths who as a class tend to exhibit a theta rhythm in the resting records, prolonged administration of amphetamine assisted in readjustment, but there was no correlation between the presence of theta rhythm and the success of the treatment; whatever the E.E.G. pattern, it was little affected by the drug. An abnormal E.E.G. does not contraindicate electric shock therapy (Taylor and Pacella, 1948), which is generally agreed to produce reversible changes in the records similar to those found after concussion (Cornil, Gastaut, Ollivier and Cain, 1946; Cremerius and Jung, 1947; Gottlieb, Knott and Kimble, 1948; Moriarty and Siemens, 1947; Rubinstein and Kurland, 1947; Weil and Brinegar, 1947). As in the case of insulin treatment, the E.E.G. can be used as a monitor (Cornil, Gastaut and Ollivier, 1945). Provided that treatment is not carried on too long, the records return to normal in a month or so; the first few convulsions have the greatest influence (Hoagland, Malamud, Kaufman and Pincus, 1946).

The effect of leucotomy is variable and correlates little with the clinical results (Cohn, 1945; Davis, 1941; Greville and Last, 1947; Hertz, 1947; Stevens and Mosovich, 1947). In general, but by no means always, there is an increase in alpha activity after the operation, and a decrease in the proportion of components at frequencies above 14 c/s. Not all cases show delta activity even immediately after the operation, but when this is present it is more prominent anterior to the section, and is often synchronized in the two frontal poles. This suggests that the slow activity is due to partial isolation of the cortex rather than to local damage. Even when prominent immediately after the operation, delta activity disappears within a matter of months. The most frequent finding is an increase in amount and proportion

of theta activity at a frequency of 5 to 6 c/s and more prominent in, but not localized to, the frontal regions. This theta activity is not correlated with specific mood or personality changes, and seems likely to be due to the physiological effects of the section. Detailed correlation of post-leucotomy records with the subtle and irregular changes in autonomic balance and affect would be of considerable interest. (Rinkel, Greenblatt, Coon and Solomon, 1947; Reitman, 1947.)

Some interesting but rather puzzling observations on the influence of shock therapy on the high frequency activity induced by sodium amytal in schizophrenia and depression have been reported by Gottlieb, Knott and Kimble (1948); the interesting paradox is presented that clinical improvement induced by E.C.T. is accompanied by a decrease in the fast activity in the E.E.G., while transient improvement induced by sodium amytal is associated with an increase in the higher frequency components. When the two treatments were combined, the anaesthetic produced less high-frequency activity than when it was used alone. It is tempting to infer that the benefit of shock therapy is due to the protracted inactivation of short feed-back circuits in the frontal lobes, while the more evanescent effects of amytal may be attributed to their temporary-fatigue. It is apparent, however, that in mental disorders, as in epilepsy, there is little hope of tracing aetiology or therapeutic success to a single neurophysiological entity. Even in patients with such a well-defined symptom as migrainous headaches the E.E.G. picture is variable, though more useful data are obtained if the examination can be made throughout or at various phases of an attack (Dow and Whitty, 1947), and clearly a number of factors are involved. Busse (1947) obtained records from patients with skull defects following head injury, suggesting that there was some correlation between traumatic amnesia, pronounced delta activity and severe post-traumatic headache, but there was no general correlation between abnormality as a whole and complaint of headache. These findings would seem to be due to the coincidence that very severe injuries are almost certain to produce tractive scars and cerebral lesions; moderate ones may produce one or other or both of these effects, depending upon other factors.

Some of the difficulties in applying the E.E.G. to the diagnosis of epilepsy have been reviewed by Diethelm (1947), Jasper (1947), and Lennox and Davis (1947); its importance in the diagnosis of the nature of attacks in children has been emphasized by Cornil, Cremieux and Gastaut (1948), and the correlation between clinical and E.E.G. features has been analysed by Abbott (1947). Stimulation by various means has greatly increased both the diagnostic efficiency of the E.E.G. and understanding of the epileptic mechanisms (Jasper and Drooglever-Fortuyn, 1946). The most useful "activators" seem to be metrazol (Kaufman, Marshall and Walker, 1947; Cure, Rasmussen and Jasper, 1948; Ziskind, Sjaardema and Bercel, 1946), insulin hypoglycaemia (Baissett *et al.*, 1948), and photic stimulation (Gastaut, Roger and Gastaut, 1948; Walter, 1946; Walter, Dovey and Shipton, 1946; Walter and Walter, 1949a; Walter, Walter, Gastaut and Gastaut, 1948). Water intoxication was less discriminatory, evoking low frequency activity in both normal and epileptic subjects and leaving some in both groups unaffected (Cohn, Cobb and Mulder,

1947). The special electrical and anatomical features found in psychical seizures have been considered by Penfield (1947), and a particularly well observed case of musicogenic epilepsy had been described by Shaw and Hill (1947).

The distinction between purely psychiatric disorders and conditions in which mental symptoms arise from organic disease is often assisted by E.E.G., particularly when repeated examinations can be made (Coma—Bugnard, Fischgold, Delcambre and Bounes, 1947; Arsenical encephalopathy—Engel, Romano and Goldman, 1946; Encephalitis—Gibbs and Gibbs, 1947; Poliomyelitis—Goldbloom, Jasper and Brickman, 1948; Trauma—Laufer and Perkins, 1946, 1947; Roseman, 1947; Organic cerebral disease in general—Baudouin, Puech, Fischgold and Brisac, 1947; Walter, Hill and Williams, 1948).

As has been emphasized in several connections, the electrophysiological basis of mental mechanisms and particularly the study of mental disorders, cannot be regarded as a search for simple equations or syllogisms. Already some of the most interesting observations are difficult to express in straightforward terms; if they were all of an exact and quantitative nature, the data could perhaps be represented in a mathematical form, which would accommodate their many parameters and dimensions. But most observations in this field are still approximate and qualitative, and, of course, include errors and aberrations induced by a multitude of uncontrolled variables. Some objectives seem most likely to be reached by envelopment rather than attrition. There is no reason why the many facets of cerebral function should not all be allowed to reflect a spark of information, nor should the varying hues of individuality be dismissed as tiresome complications. It is axiomatic that one of the main activities of the central nervous system is to generate new functions of many variables, and the electrophysiology of such processes can only be studied by combining the disciplines of many schools. The formation of conditioned reflexes, for example, must have some physical correlates, and it would be surprising if some of these were not electrical. Livanov and his colleagues (1938, 1940, 1945) claim to have recorded specific electrical changes in the brains of animals during the conditioning of a new response. They synchronized a rhythmic painful stimulus with neutral visual or auditory stimuli and recorded the electrical changes in the motor, sensory and visual areas. During the early trials the activity evoked in these areas was distinct and separate, but as the experiments proceeded large fields between them became active at the stimulus frequency even before the unconditioned stimulus was applied. Later the rhythmic activity became restricted to the projection area for the conditioned stimulus and that of the effector, and at this stage the conditioned response appeared. It is claimed that the various laws of Pavlovian conditioning could be followed in electrical terms.

In man, such experiments are very much more difficult both because the E.E.G. voltages are so much lower with transcranial leads and because control of the significant stimulus level is more uncertain. On the other hand there is the important advantage that subjective as well as objective data can be collected. In order to distinguish evoked and modified rhythms from spon-

taneous ones, stimuli can be derived from the various components of the E.E.G. itself by means of special trigger circuits (Walter, Dovey and Shipton, 1946; Walter and Shipton, 1949; Shipton, 1949). With this device appropriate stimuli in any mode can be synchronized with any desired phase of a selected component of the electrical activity. When the stimulus is locked on to a rhythm which is entirely autonomous, stimuli will appear at the frequency of the rhythm, but varying the phase and time relations between the triggering rhythm, and the stimulus does not affect the record. Conversely, if the initiating rhythm and the stimulus are connected in any way, then adjustment of their phase-relations will determine whether the feed-back is positive or negative. When there is positive feed-back the cerebral rhythm will be maintained or augmented; when negative it will be suppressed. This arrangement is particularly effective for evoking seizures in predisposed subjects; when photic and auditory stimuli are used together, the evoked abnormality can be augmented or reduced by altering the time-relations between the stimuli, as well as by changing their phase-relations with the trigger rhythm.

In some normal subjects the simultaneous application of rhythmic visual and auditory stimuli has been found to exert a mutually facilitating action on the evoked rhythms (Gastaut and Corriol, 1948), and this facilitation appears to outlast the duration of the stimulus with distinct signs of something like the effect described by Livanov and Poliakov (1945).

In some cases of psychoneurotic or psychopathic disturbance, rhythmic sensory stimulation has a dramatic effect closely resembling the induction of an epileptic seizure, even when there is no clinical evidence or complaint of attacks (Walter, 1950). In such cases the details of excitation can be worked out by using the trigger feed-back device to drive a visual and auditory stimulus from the evoked cerebral discharges themselves. When the two types of stimuli are correctly adjusted in their phase relations to one another and to the evoked activity, a temporo-occipital discharge of the "slow spike and long wave" or "sharp wave" type is evoked every few seconds, the patient making no complaint. If the time relations of light and sound are changed, this effect disappears, though the light alone can still evoke a transient "sharp wave" response. Further, if the external feed-back circuit is connected through a resonant circuit, this seems to act as a flywheel, for instead of the isolated transients, a crescendo of frontal spikes and muscular jerks ensues, sometimes ending in a convulsion and always accompanied by disagreeable sensations. This is further evidence that the brain can protect itself by a distinctive slow "blanking" wave when involved in a system which tends to be inherently unstable through positive feed-back, but cannot so easily resist the influence of such an arrangement when the blank period is occupied by powerful external stimuli at the frequency at which oscillation tends to occur. It may help toward the eventual understanding of the nature of epilepsy and its relation to psychic disturbance if one considers such cases as demonstrating how, by physiological means a *petit mal* pattern can be converted into a *grand mal* one by, so to say, raising the damper on a single note of the chord. In non-epileptic subjects the transition is usually accompanied by disagreeable sensations and sometimes by psychotic behaviour, suggesting that the difference

between the various forms of epilepsy and mental disturbance may be a matter of physiological detail and degree rather than of fundamental pathology.

The conditions set up by powerful rhythmic stimuli sometimes seem so peculiar that it is difficult to accept them as having any close relation to normal function, but careful inspection of the records shows that nearly always the most bizarre evoked activity has frequency and time relations of its own—it is not merely a succession of individual responses, but an augmentation by resonance of some immanent process. In general, the more remote is a response from the primary visual fields (in the case of photic stimuli) the less straightforward is its relation to the frequency and time relations of the stimulus, and at the same time, the more complex and irrelevant are the subjective and somatic correlates. There is often a slow increment as the stimulus is applied and a ~~long~~ persistence when it is removed. Thomas (1950) has found that when records of psychotic patients are carefully analysed the effect of a stimulus at a certain frequency may persist for upwards of ten seconds, even when the stimulus is continued at a different frequency. The possibility of such long after-discharges suggests that some types of short-term memory and prediction may be achieved in this compact and flexible form.

Experiments of the sort outlined put a considerable strain on the resolving power of even the most elaborate modern equipment. To study mental phenomena in their proper detail novel techniques must be developed; their application to problems of psychiatry opens up a wide and almost virgin field for diligent and well-equipped teams of experimenters.

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CYBERNETICS.

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CYBERNETICS may be defined as the branch of science which studies, in complex mechanisms, the *lines of communication* which may be established between part and part, the *information* which may be transmitted along them, the *control* which each part thereby establishes over the other, and the *co-ordination* which is thereby achieved.

The word was coined by Prof. Wiener in 1948 from κυβερνήτης — a steersman. The derivation is appropriate, for from time immemorial steering has been an outstanding example of the control of one system by another. Its Latin corruption, yielding "governor," recalls that the first mechanism designed to be self-correcting was Watt's governor for steam engines.

Some word had to be coined because, during the last twenty years and particularly during the later years of the war, a great body of new knowledge had come into existence dealing, in complex mechanisms, with the processes of control and co-ordination. War forced the development of many mechanisms remarkable in their activities not for great force but for great complexity: aircraft predictors, automatic pilots, automatic computing gun-sights, automatic radar-controlled searchlights and guns, and many others. Experience began to show that mechanisms apparently very different might be subject to common principles. It was found, for instance, that the "information" provided by a system could be measured quantitatively; that the provision of "feedback" gave the mechanism altogether new potentialities; and that feedback wrongly applied could lead to disastrous instability. These common principles are the subject of cybernetics.

The most complex mechanisms yet made are the modern electronic computing machines. The student of cerebral physiology cannot wholly ignore them for the following reason: all behaviours of living organisms can be represented, apart from subjective aspects, as actions; every action can be represented as a form of computation (Ashby, 1947a); all computation can be reduced to a basic set of operations (Turing, 1936), all of which can be performed by the modern computing machine. It follows that *the computing machine*, subject to the limitation of size only, *can represent every objective "mechanistic" activity of the living organism*. Increasing experience of the properties of these machines has convinced most workers that their activities can throw light on the corresponding activities of the brain. "We feel" says Jefferson (1949) "perhaps that we are being pushed . . . to accept the great likeness between the actions of electronic machines and those of the nervous system." It is probable, therefore, that the principles established in the design and performance of these machines may help us to understand the mechanisms of the normal brain.

Cybernetics, however, goes further than this. Although the machines were of various types, it was found that their faults tended to show some uniformity. It was found that all machines, as they became more complex, tended to develop almost uniform faults. Complex machines developed disorders not possible in the simple; and all the complex tended to develop them. Mere complexity seems to have its own "pathology" quite apart from the practical details of the particular machine. (An example will be given later.) Since the brain, as a machine, is even more complex than the computing machines, present knowledge suggests that these disorders may have their counterpart in the brain. Certainly everything that is known at present makes one wonder how the brain ever manages to avoid them, so similar in some ways are the modes of action of brain and computing machine. It is not impossible that cybernetics may make substantial contributions to our knowledge of the disorders to which the cerebral mechanisms are subject.

One word of comment. Since thermionic valves were used by many of the machines mentioned above, cybernetics started as a branch of electronics, but the association was incidental. The study now ranges over all complex systems whose total behaviour depends on the action of part on part; among these, by the action of neuron on neuron, must be included the nervous system.

CONTROL.

In the past, much confusion has been caused by the fact that when, in a simple machine, part *A* controls part *B*, *A* often has to provide the energy for *B*'s action. So the fact that *A* controlled *B* often implied that *A* supplied energy to *B*. The implication is now known to be devoid of fundamental importance; for when free energy is supplied abundantly to every part, the direction of flow of energy has no necessary relation to the direction of the control exerted. It is, in fact, possible for the flow of both energy and matter to be from *B* to *A* and yet for *A* to control *B*. Previously, some distinction was made between the two cases when *B* did and did not possess its own source of energy. If *B* derived its energy from *A*, *A* was said to "drive" or to "force" *B*, while if *B* had its own source, as was usually the case in living systems, *A* was said to act as "trigger" to *B* or to send *B* a "signal" or "message." In general all these words have the same factual content, and they all refer to the same primary event. *A* "controls" *B* if *B*'s behaviour when *A* has the value A_1 is not the same as *B*'s behaviour when *A* has the value A_2 . This concept, defined as a practical test, is fundamental.

The relation between *A* and *B* can be stated more precisely thus. Any system whose behaviour is determined by its state at a given instant can be specified by a set of simultaneous ordinary differential equations of the first order. If the system has variables $x_1, x_2, \dots, x_n$ then

$$\frac{dx_i}{dt} = f_i(x_1, x_2, \dots, x_n) \quad (i = 1, 2, \dots, n) \quad (1)$$

and so long as the system is free from arbitrary interference, the f 's will contain no functions of the time other than $x_1, x_2, \dots, x_n$. It follows that their integrals

$$x_i = F_i(x_1^{\circ}, \dots, x_n^{\circ}; t) \quad (i = 1, \dots, n) \quad (2)$$

(where $x_1^{\circ}, \dots, x_n^{\circ}$ is the state at $t = 0$), regarded as a substitution transforming $x_1^{\circ}, \dots, x_n^{\circ}$ into $x_1, \dots, x_n$, form a finite continuous (Lie) one-parameter group. If the system can be controlled by other variables $a_1, \dots, a_m$, the functions f_i will contain parameters $a_1, \dots, a_m$ whose values will determine the functional dependence of the f 's on the x 's. As these parameters will appear in the f 's, so will they affect the behaviour of the system. If the x 's belong to system B while the variables of system A are $a_1, \dots, a_m$ having equations

$$\frac{da_i}{dt} = g_i(a_1, \dots, a_m) \quad (i = 1, \dots, m)$$

then the conjoint equations represent the double system of "A controlling B":

$$\begin{cases} \frac{da_i}{dt} = g_i(a_1, \dots, a_m) & (i = 1, \dots, m) \\ \frac{dx_i}{dt} = f_i(x_1, \dots, x_n, a_1, \dots, a_m) & (i = 1, \dots, n) \end{cases}$$

The integrals of the conjoint equations will show how the a 's are controlling the x 's. In particular, if $x_p = F_p(x^{\circ}, a^{\circ}; t)$, where x° and a° represent the whole

set, x_p will or will not be independent of a_q as $\frac{\partial}{\partial a_q} F_p(x^{\circ}, a^{\circ}; t)$ is or is not identically zero, respectively.

The degree of control which one system exerts over another can be measured quantitatively. Thus suppose A can take, as a variable, only two values. Then B can show only two reactions, though each may be very complex. An approximate example is given by the reactions to a single sex-hormone which is effective only in the two degrees "present" or "absent." In such a case the animal will show two types of sex-response. The immature female rat, for instance, shows a characteristic avoiding reaction if approached by the adult male; but if an injection raises the blood-oestrogen above the threshold level, this reaction is replaced by the characteristic mating reaction (Beach, 1948).

The amount of control which A can exert over B depends, not on the complexity of A nor on its "force" but on the number of values which A can take as a variable; *it is measured by the logarithm (to the base 2) of the number of values*. Thus, however complex the oestrogen molecule, if its levels of concentration in the blood are effectively only two, then only a pair of reactions can be controlled by it. And the amount of control exercised by it is 1 unit. *If there are n variables, each able to take only two values, they can control just 2^n reaction patterns*. The amount of control then exercised is n units.

INFORMATION.

For some purposes, especially if we are concerned with only the first stage of the control, it is convenient to ignore the controlled system and to regard A simply as emitting "information." Much of cybernetic theory is stated in

this form. The previous section will have made clear that "information" has no metaphysical implications, but measures simply what is provided for the control of the next stage.

A fundamental advance was made when it was realized that the information carried by any message is obtainable only by a comparison of the actual message with all the other messages which might have been sent but were not. *We must consider not the message but the statistical ensemble.* The statement becomes obvious when one thinks of the cables which can be sent as a single code-number taken from a list. No matter how verbose the final form, it conveys no more information than can be obtained from a comparison of the selected number with the rejected. If the list contained only two numbers, for instance, then no message could convey more than one unit of information. But though obvious in this form, the statement is by no means trivial; for it immediately relates the subject of "messages" to that of statistical mechanics. This branch of science, which also treats the individual event only against the background of the ensemble, has a well developed technique: all this is now available for studying the transmission of messages.

The amount of information in a message can be measured—this was a first result of the new method. Fisher (1948) has given a measure of the amount available for the statistical estimation of a parameter, but his measure, though related to, was not identical with Wiener's. The unit of information—a "decision"—is a distinction between two equally likely possibilities. Since a message telling which of 2^n possibilities has happened can be conveyed by n decisions, it will be seen that *a message telling which of k equally likely possibilities has happened contains $\log_2 k$ units of information.*

The measure implies that if A sends information to B through some channel, and if the number of channels is increased, then the amount of information which can be transmitted is increased proportionately. But it can also be shown that a single variable between A and B can transmit an amount of information limited only by the variable's power to fluctuate, so that its first, second, and higher derivatives with respect to time can act as independent variables.

As an example of the use of this measure, I will cite the treatment of "noise." Every complex and active machine tends to suffer from some degree of random, uncontrollable variation introduced by the statistical nature of molecular and electronic activities: the basic random activity is usually referred to as "noise" (from its audible effect in radio). Its effect in the nervous system has not yet, so far as I am aware, been studied systematically. In predictors, however, where it tends to confuse every action, it has been studied intensively. By using the measure of the amount of information, the designer was able to study its effect on prediction; thus he could so adapt the values of the disposable constants that the quantity of information emitted to the next stage was maximized.

When the effect of noise, i.e. of random non-significant changes, comes to be studied in the nervous system, the techniques of cybernetics must provide the first line of attack. Such a study may well yield results of high practical importance if only because it treats the nervous system more realistically.

The animal in the physiological or psychological laboratory, subjected to a few exactly controlled stimuli, is by no means typical of the free-living organism; for the latter is incessantly bombarded by stimuli of which often only a minor part is significant for the animal's welfare, yet all the other stimuli pour into the nervous system and require neutralization. During the neutralization, the brain must distinguish, as does an aircraft predictor, between the significant and the random. Information once lost or destroyed can never be recovered; in this respect, as Wiener has shown, it behaves quantitatively as the negative of an entropy.

STORAGE OF INFORMATION.

The more complex mechanisms commonly need some means by which the results of one part's activity can be delayed and stored; for different parts, undertaking different actions, will usually differ in the times they take to complete their portion of the whole task. Such delays may extend from fractions of a second to many hours. During this time, the result of the first part's activity must be maintained invariant but available. Such a delay is now generally referred to as a "memory." The name seems unobjectionable provided it refers only to the objective fact of retention.

Many simple devices can be used when only a brief delay is required. In electronics the theory of "clamping" is well established (James *et al.*, 1947). More interesting are the longer-term storage mechanisms, now raised to a high degree of technical perfection in the computing machines. Though there is danger in following their practice too closely, it is of interest to note that two basic types have been used; nor is it easy to see how any other essentially different type is possible. The first type is static: the events cause some localized structural changes which persist indefinitely. Thus in one machine the events are punched automatically on to cards, and at some later time the perforations determine how the next stage shall act. Other methods are the tripping of switches or relays, and the photographic. In the brain such static mechanisms would correspond to changes localized in neurons, so that each one's behaviour was more or less permanently affected; at present very little is known about such possibilities. The second type is the dynamic: very different in principle, for here what persists is a process. Thus, in one machine the events are transformed into a wave-pattern which is transmitted through a column of mercury; on arrival at the other end of the column the wave-pattern regenerates the series of events, which again starts the wave-pattern at the top of the column. In this way the series of events is maintained in existence over perhaps hours, the representation existing as a process whose pattern circulates. The second type has an obvious advantage over the first: the same structure can be used successively in any number of reactions, for at any moment the process can be stopped and a new pattern set circulating. In the brain such a process would require the establishment of reverberating neuronic circuits.

It seems likely that these two processes are the only two possible. If this is so the mechanisms underlying memory in the brain must also be of these types.

CONTROL BY PATTERN.

If one part is to control another, and if the parts are highly complex, the second part will often be required to respond to a certain *pattern* of events in the first, no matter how the pattern happens to be sited. In human beings the power of recognizing a given pattern in spite of changes of position, orientation, colour, or other variations is well known. The importance of *Gestalt*-recognition needs no emphasis.

For a time it was thought that such a power could not be shown by mechanism, but it is now known that the more complex machines can undoubtedly achieve it. The first step was taken by Pitts and McCulloch in 1947 when they recognized that the essential feature is that *the behaviour of the mechanism must be invariant for the group of transformations generating the equivalent representations*. Conversely, any mechanism whose behaviour is invariant for the operations of the particular group, but not for others, will show the property of *Gestalt*-recognition.

More precisely, using the same notation as above, if the machine has a resting state $X_1, \dots, X_n$, at which

$$F_i(X_1, \dots, X_n; t) = X_i \quad (i = 1, \dots, n)$$

then, if displaced from these values to $X_1^o, \dots, X_n^o$ and released, the x 's will show some pattern of behaviour depending on the values of the X^o 's. If there is *Gestalt*-recognition, the behaviours from certain sets of values $X^{o'}$, $X^{o''}$, etc. will be equal, so

$$F_i(X^{o'}; t) \equiv F_i(X^{o''}; t) \equiv \dots \text{etc.} \quad (i = 1, \dots, n)$$

In other words, the F 's are invariant for those substitutions

$$X^{o''} = \varphi_1(X^{o'})$$

$$X^{o'''} = \varphi_2(X^{o''})$$

etc., which convert the equivalent patterns into one another. *These substitutions form a group*. Since the F 's are to be invariant, the machine itself, specified by the f 's, is specified only in that the integrals of the f 's are to be invariants of the φ 's. The same *Gestalt*-recognition may therefore be achieved by a variety of mechanisms.

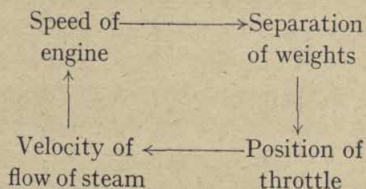
The construction of all possible invariants is not usually easy, but one method capable of wide application is that of *group-scanning*. If the mechanism, given a pattern, generates from it all the other equivalent patterns, and then reacts only to the total set, its reaction will be characteristic of that type of pattern, but will be independent of which individual pattern originated the set. Such a method might well be used in the visual and auditory cortices for pattern recognition; and, in the scanning, the alpha-rhythm may well play a part; but these possibilities are still under investigation.

FEEDBACK.

In the preceding discussion the relation between the parts was simply that A controlled B . Though necessary as an introduction, this relation has

ignored what is perhaps the most potent source of new properties in the new mechanisms: the presence of feedback. In a dynamic system, *feedback is present if the controls of part on part form a re-entrant circuit*. Thus if A controls B , and B controls C , and C controls A , then feedback is present. An equivalent definition states that it is present if we can find a pair of subscripts j and k such that F_j contains x_k^o , and F_k contains x_j^o . It will be noticed, as mentioned above, that what is fed back is neither energy nor matter, but control or information.

The Watt's governor provides a clear elementary example. If we use the symbol $A \rightarrow B$ to mean " A controls B ," then the Watt's governor has the control-flow chart



Each arrow refers to a specific and demonstrable control in the machine. Take the top arrow as example: the speed of the engine, however caused, determines the separation of the weights (by centrifugal force) independently of the position of the throttle, and of the flow of steam. On the other hand, the speed of the engine has no effect on the position of the throttle other than that exerted through the separation of the weights; for if the separation is fixed, the speed has no effect at all on the throttle; there is, therefore, no arrow going down to the right. The other arrows may be examined similarly. The controls therefore form a re-entrant circuit; and this circuit can be demonstrated objectively. It is important to notice that the assignment or not of feedback to a system is no matter of opinion or of a point of view—its presence or absence can be determined objectively.

Until about 1930 few machines contained feedback. So to the psychologist the concept of "machine" tended to be that of "machine without feedback." The restriction was encouraged by the fact that the physiologist often, or even usually, destroyed feedback in his experimental animal as a necessary simplification prior to experiment; for the relation of part to part cannot be investigated while they are acting within an active whole. But the destruction of the feedback delayed the appreciation of its remarkable properties.

Its importance is due to the fact that machines with feedback have powers fundamentally unavailable to machines lacking it. Thus, it used to be thought that machines could not correct their own errors—if feedback is absent this is true, but not otherwise. *Machines with feedback can correct their own errors; the same fact means that they can be goal-seeking*. This discovery will probably revolutionize cerebral physiology, for it provides a mechanism altogether more flexible and adaptable than those hitherto considered.

There seems to be little doubt that circuits with feedback do exist in the nervous system. Lorente de Nó (1933) provided clear histological evidence of their existence. He found them to be so widespread that he enunciated a Law

of Reciprocity of Connexions: "If a cell-complex *A* sends fibres to cell or cell-complex *B*, then *B* also sends fibres to *A*, either direct or by means of one inter-natal neuron." It is only recently that the full significance of this observation has been appreciated.

Within the body, feedback systems are common. All the homeostatic mechanisms, for instance, use it. Consider, for instance, the facts that the pH of the blood controls the activity of the respiratory centre, that this activity controls the rate at which CO_2 is removed from the blood, and that this rate controls the pH of the blood—the re-entrant circuit is clear. Again, activities like walking usually use feedback, for at each moment the next muscular movement is controlled by the sensory impulses returning with information about the results of the preceding movement. The inco-ordination of *tapes dorsalis* is due to loss of this information. The ataxia may correctly be ascribed to the loss of feedback, for, as is well known, if the lost kinaesthetic feedback is replaced by visual information the ataxia is markedly reduced.

Feedback also occurs in the interaction between animal and environment (Ashby, 1940; Rosenblueth, Wiener and Bigelow, 1943). But these feedbacks are so complicated that the concept of a single circuit is inadequate—in these cases a more complex method is necessary (Ashby, 1947*b*). But of the fact there can be no doubt: "The good player of a quick ball game, the surgeon conducting an operation, the physician arriving at a clinical decision—in each case there is the flow from signals interpreted to action carried out, back to further signals and on again to more action" (Bartlett, 1947).

GOAL-SEEKING BEHAVIOUR.

Perhaps the most important property of systems with feedback is that the system can become actively goal-seeking. The word is used with no meta-physical or subjective implication, but simply to describe an objective form of behaviour. Thus a simple feedback circuit like Watt's governor automatically returns to a central, set speed no matter how it is displaced. Such systems show the property in only larval form: more complex systems can show it more dramatically. Thus one type of automatic radar-controlled anti-aircraft gun uses the pulses returning from the target aircraft and from its own shells to alter its direction of aim so that the distance between shell and target is minimized. Such a mechanism will follow the target in spite of all manoeuvres and will correct its aim continually. It behaves exactly as if it were trying to get its shells on the target. After each shell it uses the information about its error so as to reduce the error of the next shell. Goal-seeking behaviour, then, is the prerogative, not of the living system, but of the system with feedback.

Such self-correction is a primary necessity for living, and the homeostatic mechanisms show this property without exception. Thus at every moment the deviation of the pH of the blood from about 7.3 acts as cause for the correction of the deviation. The deviation of the body temperature from about 98° F. acts as cause for the correction of the deviation. The "self-regulating" properties of these mechanisms are identical with the "goal-seeking" properties of systems with feedback.

Homeostasis in the vegetative mechanisms works mostly within the body, but some of these mechanisms make use of the external world for their self-regulation. Sweating, for instance, uses the drying properties of the surrounding air. In the free-living animal there is only a difference of degree between those vegetative activities by which it maintains homeostasis in the narrow sense and those somatic activities by which it uses the environment for homeostasis in the wider sense. The sole difference is that in the latter the feedback circuit is longer, more complex, and includes the environment. It seems likely, therefore, that a large part of normal behaviour will eventually be treated by cybernetic principles.

STABILITY.

The provision of feedback gives to a system, as we have seen, great new powers. But with them comes a new possibility: the system may be unstable; for feedback, if improperly arranged, will make the error not self-correcting but self-aggravating. As a simple example, consider a Watt's governor with one part reversed, so that an increase in speed makes the throttle open wider; such a system will diverge from the normal value instead of converging towards it. In all feedback systems stability is of prime importance.

A system is stable if to a bounded disturbance it produces a bounded response. Contrasted is the unstable, which is no sooner started than it develops a "run-away." It should be noticed that stability in no way implies immobility, though it often happens that change will not be shown except in reponse to a disturbance.

Stability is a property of the whole system, and belongs to no part of it. For this reason, in any question of stability the system must be treated as a whole; for no examination of the parts separately can answer the question. Thus a number of parts each individually stable may form a whole which is unstable. And unstable parts may actually combine to form a whole which is stable. Again, parts may be joined to form a whole which is stable if the parts are joined in one way, but unstable if joined in another (Ashby, 1947b).

Related to this is the fact that stability can be achieved only by a proper co-ordination between the parts. As an extremely simple example, suppose, in the homeostatic regulation of the pH of the blood, that as the pH fell the respiratory centre became *less* active—the reverse of the normal arrangement. Any deviation from the normal pH would now be self-aggravating instead of self-correcting. Such an animal would soon destroy itself either by hypopnoea with a low pH or by hyperpnoea with a high pH. If, however, CO₂ gave an alkaline solution, this relation between breathing and pH would be the correct one. Thus a reversal of action at one stage in the feedback circuit can be compensated by another reversal at another stage. The stability of the whole circuit depends on the proper co-ordination of all the stages.

For this reason, the more complex the feedback the more complex the co-ordination needed for stability, and the more difficult its achievement. Though it is not yet possible to make an exact statement, we know enough to say that *all large systems with much feedback should be regarded as unstable unless there is evidence to the contrary.*

A resting state $X_1, \dots, X_n$ is one at which $f_i(X_1, \dots, X_n) = 0$ ($i = 1, \dots, n$) and at which $F_i(X_1, \dots, X_n; t) \equiv X_i$ ($i = 1, \dots, n$). The stability at such a state may be investigated by the well known theorem that *in the neighbourhood of a resting state the equations (1, above) tend to the linear form*:

$$\frac{dx_i}{dt} = a_{i1}x_1 + a_{i2}x_2 + \dots + a_{in}x_n \quad (i = 1, \dots, n)$$

where $a_{jk} = \partial f_j / \partial x_k$ taken as its numerical value at $X_1, \dots, X_n$. A linear system is stable if and only if all the latent roots of the matrix $[a_{jk}]$ have negative real parts. Since the values of the roots depend not only on all the elements a_{jk} , but on all the relations between them, the statement that stability is a holistic property can be given an exact meaning. Routh's (1905) method, modified by Frazer and Duncan (1929), enables the test to be made without explicit computation of the roots.

This method for testing a system's stability is widely applicable, but in the special case of the linear system it is often simpler to use its transfer function

(James *et al.*, 1947). The Laplace transform of $f(t)$ is $\int_0^\infty f(t)e^{-pt} dt = Lf(t)$. It

can be shown that, for a given system, the ratio of the Laplace transform of the output to the Laplace transform of the input which caused it is a constant function $Y(p)$ —the transfer function. It follows that if we know a linear system's output (or response) to one input (or stimulus) we can at once calculate its response to any other stimulus. Thus, if a unit step-function input caused an output $S(t)$, then any other input $Q(t)$ would give the output

$$L^{-1}\{p.LS(t).LQ(t)\}$$

where L^{-1} is the transformation inverse to L .

The transfer function $Y(p)$ can also be readily obtained from the practical details of a system. The stability of the system can be related directly to $Y(p)$, for a system is stable if and only if $Y(p)$ has no poles in the right-hand half of the complex p -plane or on the imaginary axis. If the system is doubtfully stable, Nyquist's (1932) criterion usually gives clear guidance.

Wiener (1948) has given an interesting application of these principles to the physiological control of hand-movements. The position of the hand depends on the degrees of flexion of shoulder, elbow and wrist successively, each acting as basis for the movement of the next more distal joint. The cerebral cortex can control hand-position only by acting through all three. To control a variable through three intermediaries is not easy. Exactly the same difficulty confronts the helmsman, who controls the helm, which controls the steering engine, which controls the position of the rudder, which controls the direction of the ship. Since this direction determines the next action of the helmsman, feedback is present. It involves several independent stages. Ship-builders have long known that such a system is difficult to keep stable, but that it can be stabilized by the insertion of subsidiary feedbacks within the main circuit. An exact example is that given by Wiener, who considers the properties of a system built by joining, in series, units each of which has the transfer function

$Y(p) = 1/(1 + kp)$. If n such systems act in series, and if there is an overall feedback with transfer function λ , then the whole system will have transfer function—

$$\frac{1}{(1 + kp)^n - \lambda}$$

It is easily shown, by using the test given above, that if k is positive, i.e. if each unit is intrinsically stable, then if the chain is only two units long, the whole may easily be made stable by making λ large and negative, i.e. by using plenty of negative feedback. But as the chain lengthens, our power to stabilize it becomes more and more restricted. When there are three units, for instance, the negative feedback may not exceed 8^* or the system will again become unstable.

Exactly the same principle applies to the arm. It is therefore to be expected that inco-ordination in the hand-movements will occur if the subsidiary postural reflexes controlling the intermediate joints are destroyed, even though the direct overall feedback from hand to motor cortex is intact. It is easy to predict what will happen in such a case when the patient attempts to reach for an object: the shoulder and elbow will move into extreme and contorted angles; but the hand, in spite of this, will eventually reach the object—for the overall feedback ensures this. Such movements are not uncommonly seen in neurological practice.

It must not be thought, as instability is usually undesirable, that stability is wholly good. It may be shown that if in a system some part is made more stable, the part tends to become less mobile and to exert less control over the other parts. Such little movement as it does make tends to be more due to the other parts than to its own inner working; it tends, in other words, to become a slave to the others. *When there is interaction, the dominating part is that one nearest to instability.* Many systems work best when they are as close as possible to instability without actually passing the boundary beyond which a runaway would start.

Excessive stability seems to be shown in some psychiatric conditions. The melancholic and the catatonic respond to little but the strongest stimuli; the inertia is *prima facie* evidence for an excessive stability in some cerebral mechanism; but the possibilities in this direction have not yet been explored. At the opposite extreme lie mania and schizophrenic excitement. Here the least stimulus may evoke a response of any magnitude. Further, the activities show a typical feature of the unstable state: the runaway does not need to be evoked by some definite external stimulus, but can be developed by the unstable system within itself. Once a patient has passed into mania, it is well known that removal of all sources of external stimulation does not usually remove the excitement, for the patient now finds ample stimulation within his own racing thoughts. Such self-generating activities are typical of the unstable state.

On the border-line between stability and instability most systems tend to show oscillation. The reason is as follows. If the latent roots of $[a_{jk}]$ are

* In Wiener's book this is misprinted as 2.

$c_1, \dots, c_n$, the behaviour will be a linear function of exponentials

$$r_1 e^{c_1 t} + r_2 e^{c_2 t} + \dots + r_n e^{c_n t}$$

having the roots as exponents. If the system changes from stable to unstable, at least one of the roots must change its real part from negative to positive. Suppose it is $c_s = x + iy$, where $i = \sqrt{-1}$ and x and y are real. At the intermediate stage the root will equal iy approximately; so the behaviour will depend on a term

$$r e^{iyt} = r(\cos yt + i \sin yt).$$

As its real behaviour now resembles $r \cos yt$, the system will oscillate with a frequency of $y/2\pi$.

In many disorders of movement, tremor is conspicuous. For this reason some have looked for special "tremor" centres, supposed to be normally inhibited, while others have wondered what special mechanism could produce the movement. It will be appreciated that no special mechanism is required: it is sufficient that the normal mechanism achieves its stability by feedback. Since a mechanism, if not properly stabilized, will almost always oscillate. Conversely, measurements of the oscillation—its constants of frequency, amplitude and decay—in clonus and tremor, are capable of giving direct evidence about the constants in the feedback circuit. Wiener and Rosenbluth have attempted to follow this line, but their results are not yet available.

CIRCULATING PROCESSES.

The abnormalities described so far are simple, depending on principles applicable to simple systems. But complex mechanisms have been found to show a type of disorder not previously observed. It is possible that this type may have some relation to the psychoses.

To understand the nature of the disorder, it is necessary to appreciate that the more complex mechanisms, and particularly the big computing machines, are arranged to have a considerable degree of internal freedom. Thus in a computer a few subsystems may be specially constructed for long division. Other subsystems requiring a long division hunt for an unemployed divider; when found, it is given the two numbers, it computes the quotient, returns the answer to the first system, and then disconnects itself. If the same main computation is repeated later, the divider used on the second run will probably not be the same as that used on the first run, for the second hunting process started with the switches as they were left at the end of the first run. Successive runs, in other words, differ in many details; but the differences do not affect the final result. The larger the machine, the more are the details left to it, to be determined at each moment by what is required and what is available.

The provision of this freedom and of "memory" gives the machine great new powers for computation, but it introduces possibilities for disorder not seen in simple machines. Thus, by some peculiarity in a particular computation, by some slight defect, or by some coincidence of timing, the machine may happen upon an action which is regenerative. Then there may arise a *circular* process which contains within itself factors tending to sustain and to preserve its own existence. Thus, just at the moment when a part *A* was preparing

to send a message to *B*, *B* might send to *A* the command "copy what I am doing." *A*'s message to *B* would then be "copy what I am doing"; so *B* would re-transmit it to *A*; and the circular process, the vicious circle, once started, would be self-perpetuating.

The reader will appreciate that such circular processes are in no way peculiar to electronic machines. Any mechanism will be liable to them if it consists of large numbers of parts interacting in a network which contains many paths for feedback. A network of neurons must also be liable to such circular processes. Even if the nervous system contained no internal feedbacks—if every path was always in the direction from sensory to motor nerves only—the possibility of circular disorders would still be present; for the free-living organism has an active environment which will provide feedback by conveying effects from the motor organs to the sensory receptors, for every motor action has sensory consequences. It will be seen that the free-living organism must be liable to abnormal regenerative circular processes.

Since this type of disorder has been recognized only recently, its main characteristics will be described.

First, since an increase in the size and complexity of a mechanism will increase the number of possible circuits, this type of disorder will appear more readily in the more complex mechanisms. Secondly, as more freedom is allowed to the mechanism in its processes—that is, as the mechanism is made more flexible and adaptable—so will the likelihood of the occurrence of a circular disorder increase. Thirdly, the more the mechanism becomes goal-seeking and self-correcting, the more must feedback be introduced into the internal arrangements; and this increases the likelihood of a circular disorder commencing. It will be seen, therefore, that in general the bigger the mechanism, the more adaptable its processes, and the more it is actively goal-seeking, then the greater will be its tendency to develop circular disorders.

These, of course, are not the only factors controlling the likelihood. To the computing machines various devices are added for their correction. And in man it is likely that natural selection has developed a number of methods to protect the brain against their occurrence. Failure of these methods would not show directly, but only by the occurrence of circulating disorders. In man, the location and identification of these stabilizing devices or factors are tasks for the future.

A circulating disorder affects the remainder of the system in three main ways. First, the parts used by the process are no longer available for normal use: the capacity of the machine is lowered by that amount. Secondly, any other part which makes contact with the affected parts will receive from them messages which are abnormal and distorted. The other parts, therefore, tend to be upset in their normal working; so even the normal parts cannot work properly. Thirdly, the widespread distribution of abnormal and very unusual messages provides increased opportunities for new circulating disorders to occur in new circuits. The process, therefore, does not usually remain stationary—either it disappears, or it draws all the rest of the mechanism into its orbit. Finally, it should be noticed that all this can occur in a machine which, when examined part by part, may show no sign of mechanical fault.

Electronic engineers, faced repeatedly with this type of disorder, have developed methods for its treatment. The methods have some interest since, in principle, they are capable of application to a much wider range of mechanisms than the electronic. If circulating disorders occur in the brain these methods may well prove effective. They are, in fact, strikingly similar to certain modern therapies.

A first method is to switch the whole machine off and start again. On their second run, many of the components will start from positions not the same as on their first; and some trifling coincidence which before led to trouble may not occur again. The withdrawal of the power means that any abnormal circular process will be stopped, and when the machine is restarted the parts may be swept into normal activity before they have time to re-establish the circulating process. It may be found, then, that if the machine is brought to complete rest and restarted, the trouble does not occur again.

A second method is to switch out some abnormal part in the hope that what is left will be adequate to the task. If the task is simple and speed unimportant, a large proportion of the equipment can be removed without rendering the machine useless. The complete removal of the perniciously active part may enable the whole to act with a relatively increased efficiency. If the machine is far progressed on a long task, the removal of a small abnormal part, if it enables the machine to complete its work satisfactorily, may be a more effective and practical treatment than a fresh start.

Sometimes an engineer with a thorough practical and theoretical understanding of his machine may be able to diagnose where in its depths the abnormal circuit lies. Using his knowledge he may be able to throw in an exactly devised signal which will be switched to precisely that abnormal circuit, and which will affect it in just the way he wants. His aim is to disrupt the abnormal circuit so that the parts can be linked into normal activities. Sometimes such a treatment can be achieved while the machine is actually engaged on its task. It demands, of course, an exact knowledge of the normal behaviour of the machine and an exact formation of the appropriate signal.

The final method is to put into the machine a brief but maximal electric impulse. Since these large machines are mostly self-correcting, the direct effect of the electric shock is soon removed, but after the shock it is often found that the abnormal process has disappeared. In these machines the explanation can be given with some certainty. Most of their abnormal processes are due to the accidental occurrence of circuits which are regenerative and self-perpetuating. Such circuits, being in a "runaway" condition, are usually already operating at maximal activity. A general increase in activity does no harm to processes at low activity, for they merely rise in activity from low to medium. But those already at maximal activity tend to be driven beyond the level at which some disruptive event occurs—perhaps a fuse blows—and the circuit is thereby broken. *A general increase in activity tends selectively to disrupt those activities which are already maximal.* And these, as we have seen, are usually the abnormal.

These methods of treatment have analogies with psychiatric methods too obvious to need description. Only the future can show whether the resem-

blance is a homology, and in what ways the new knowledge can advance psychiatric treatment.

LEARNING AND ADAPTATION.

So far we have considered systems whose feedbacks, though possibly complex, have worked on the same "level" as the variables. The feedbacks have depended upon various constants decided in the machine by the designer, and in the animal by its inherited gene-pattern. But if these "constants" are themselves affected by the behaviour of the system, then a higher order of feedback appears, for this second-order feedback determines the performance of the primary feedback. For us the interest lies in the fact that a second-order feedback enables a mechanism to show properties which are not otherwise possible and which show a striking resemblance to certain "intelligent" forms of behaviour hitherto found only in the living nervous system. A slight account of these new developments will be given, but space prohibits a full description.

In these higher systems a fundamental part is played by "step-functions." *A variable behaves as a step-function if its time-derivative is zero except at isolated points.* Its value, if graphed against the time, will therefore appear to change by steps, whence the name. The definition makes no reference to the cause, only to the form, of its behaviour. Its importance is due to the theorem that if a system is isolated from outside effects, and it changes from one way of behaving to another, then *the system must contain a step-function which changed value at the moment of the change of behaviour.* In the past such changes of behaviour, when produced by the nervous system, have been attributed vaguely to "switching." But this concept, drawn from the simple analogy of a train or an electric current, is too crude and restricted to represent the real change. The concept of "step-function change" is its modern and accurate form.

If the second-order feedback used "constants" which varied continuously, they would differ in no essential way from the other variables, and the system would have only a more complicated feedback, still of first-order type. But if the second-order feedback uses only step-functions, then a new type of behaviour emerges. So long as the step-functions remain constant the first-order feedback will provide a definite way of behaving; this may be stable or unstable. Under certain very general conditions it may be shown that *the second-order feedback has as its goal not the arrival at a particular state but the arrival at a stable goal-seeking way of behaving.* Such a system seems to try one way of behaving after another, rejecting those that lead to a runaway, but retaining the first that gives a stable goal-seeking way of behaving.

A machine has recently been built to illustrate this principle (Ashby, 1948). The Homeostat is a dynamic system constructed so as to behave in accordance with the equations

$$\frac{dx_i}{dt} = a_{i1}x_1 + a_{i2}x_2 + a_{i3}x_3 + a_{i4}x_4 \quad (i = 1, \dots, 4)$$

where x_1, x_2, x_3, x_4 are its main variables. It is rich in primary feedbacks, for

four variables, joined in all possible ways, form twenty interlacing feedback circuits. These are the primary feedbacks, and their nature is determined by the values of the constants a . When the a 's are set to give a stable feedback the system is actively goal-seeking and error-correcting.

Its peculiarity is that a second-order feedback is provided. The a 's are all step-functions, related to the x 's by the fact that the a 's in a row are changed suddenly to a new set of values if and only if that x exceeds a certain value. As the a 's control the x 's, and the x 's control the a 's, feedback between them is demonstrably present; and this feedback controls the pattern of feedbacks existing between the x 's.

The second-order feedback is, as might be expected, goal-seeking and self-correcting. Its "goal" is the bringing of the a 's to a pattern at which the x 's will act in a stable and goal-seeking way and not in those ways which lead to a runaway. As a result, if the primary feedbacks are altered by the experimenter, the machine will again alter them until it has restored the normal way of behaving.

It seems likely that such feedbacks are used in the brain during learning. As an animal can learn to behave in a variety of ways, the "constants" in the brain corresponding to the a 's are evidently not absolutely fixed, though they must stay constant over long intervals. They must, in other words, be step-functions. Those combinations of a -values which lead, in interaction with the environment, to unstable ways are rejected; while those that form a suitable goal-seeking combination are retained. This much can be deduced directly by cybernetic reasoning from the known facts of normal behaviour. Such behaviour can be achieved most simply and directly by second-order feedbacks.

A detailed comparison between the behaviours of the living organism and of the system with second-order feedback shows many striking resemblances. Although a great number of illustrations could be given, only two will be described.

It is commonly observed that, to the learning animal, a change in the environment causes little difficulty. Even if a specific situation which always led to food is suddenly altered so that it now leads to pain, the animal soon learns to react to the new situation with a reaction the reverse of that used for the old. A system with second-order feedback also shows such a reversal. For the reversal in the environment acts like the reversal of a part in a Watt's governor: what was stable, keeping the essential variables within normal limits, now actively drives them outside. If, however, there is a second-order feedback, goal-seeking for *stable* arrangements, the occurrence of the instability will lead to a change in the relations between the parts. It is sufficient if these changes are of random nature, i.e. determined by factors unrelated to the particular situation. For, no matter what determines their stability or instability, the second-order feedback will act by trial and error until it finds a new combination which restores the stability in conjunction with the new environment. Tracings of the homeostat's behaviour have been given (Ashby, 1949) showing that it reacts in these circumstances much as an adapting organism.

The second illustration is taken from the great class of experiments in which the animal, after a surgical rearrangement, readapts its behaviour so as to restore normal functioning in spite of the anatomical peculiarity. Thus Sperry (1947) severed the attachments of the flexor and extensor muscles in the arm of the spider-monkey and reattached them in crossed position. He found that although at first the arm movements were grossly inco-ordinated, the co-ordination improved steadily until it was almost normal. Evidently the nervous system had undergone changes compensatory to the peripheral reversal.

Such compensatory changes also occur in the system with second-order feedback. Cybernetically, the adaptation to an experimentally-induced change occurs in exactly the same way whether the change is located in the animal's environment or in the animal's limb; for the "system" treated by cybernetics is the organism and its environment considered as a whole.

CONCLUSION.

It will be seen that cybernetics makes contact with neurophysiology at many points. There can be little doubt that in the future the contacts will become more numerous and more intimate. Cybernetics has as its object the study of control and communication—both essential in integration. In the study of the principles underlying integration, cybernetics must play a leading part.

It has been found that "communication" has principles and laws which hold generally because they are intrinsic in the act of communication. Because of their generality and because the brain is a communicating system, the brain must itself be subject to these principles. Were the principles few or trivial or obvious the gain would be small; in fact, the principles are many, important and sophisticated. This extensive body of knowledge is now helping to solve the problems of psychiatry.

When old problems can be studied by a new technique, advances are often rapid and substantial. The techniques of cybernetics provide an entirely new approach to some of the classic problems of psychiatry. A new era of advances may be commencing.

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VITAMIN DEFICIENCY IN NERVOUS AND MENTAL DISORDER.

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Keys concludes that excessive enthusiasm over advances in nutritional knowledge has been tempered by the results of recent controlled studies on man, and by the collated experiences from various countries of severe malnutrition during the recent war (1). He refers to reports from Warsaw on a large population of Jews confined to the Ghetto, to Swiss and French papers, studies on large numbers of victims in German prison camps, the findings in the Netherlands famine of 1944-45, and other publications: "The essential uniformity of the findings is striking—moderate anaemia and oedema with only slight hypoproteinaemia, unexplained diarrhoea and polyuria without evidence of renal disorder, extremely little evidence for vitamin deficiencies, improved diabetes and increased tuberculosis and gastro-intestinal disorders." In the Minnesota Starvation Experiment 32 normal young men were studied for 3 months on an adequate diet, then for 6 months on a semi-starvation diet (1,560 calories), for 12 weeks on "controlled rehabilitation diets," and subsequently when on full rations. The semi-starvation diets compared closely with the "European famine pattern," and during this period a quarter of the original weight was lost and oedema occurred. Amongst the large number of objective tests employed were the psychological, referred to subsequently.

The general tendency has been to reduce the formerly accepted League of Nations calorie requirements (e.g. from 2,400 to 2,160 for the average man). Some old people in London appeared to maintain health on 1,400 calories and upwards. Key states, "the importance of calories is being rediscovered and the role of adaptation is beginning to be appreciated." Despite this broad conclusion and the negative emphasis above with regard to vitamin deficiency states, there is no doubt from numerous reports that the latter were common and widespread during the war, particularly in P.O.W. camps in the Far East.

EXPERIMENTAL DEFICIENCY IN ANIMALS, ETC.

Pantothenic acid deficiency in the chick causes widespread myelin and axon degeneration in the spinal cord, but there is no accompanying degeneration of peripheral nerves (2). In young pigs, deficiency in pyridoxine or in pantothenic acid produces a deficiency syndrome based on pathological lesions affecting the primary sensory neurones. The morphological pattern of the lesions differed in the early stages: degeneration of the peripheral process of the sensory neurone was the initial and most prominent feature of pyridoxine

deficiency; with pantothenate deficiency chromatolysis occurs, and nerve fibre changes later (3).

Thiamin-deficient monkeys showed a drop in weight, decreased food intake, general muscular weakness, loss of reflexes, convulsions, inco-ordination, increasing cachexia, signs of cardiac insufficiency, prostration, and death (4). Acute thiamin deficiency in rhesus monkeys produced a similar syndrome—diminished food consumption and loss of weight, later apathy, inactivity, weakness, ataxia, occasionally ptosis and tremor. These symptoms were dramatically removed with thiamin administration. Pathological changes found most commonly were bilateral symmetrical foci of degeneration in the putamen, caudate nucleus, inferior colliculi, cerebellar vermis and some cranial nuclei (III, VI, VIII and X). The vascular proliferative reactions described in Wernicke's disease were occasionally seen but were not prominent. No significant lesions were observed in the spinal cord (5). Gantt and Wintrobe subjected dogs, who had elaborated conditioned reflexes (100 per cent. differentiation between 2 tones), to vitamin B deficient diets, and found progressive disturbances in the conditioned reflexes in 4–15 days. The findings suggested the need for daily adequate amounts of at least some factors of the vitamin B group for optimal mental performance (6).

Chastek paralysis in foxes, caused by antithiamin enzymes contained in raw fish diet, is known to be prevented or cured by giving simultaneously adequate amounts of thiamin. Melnick *et al.* report that *in vitro* tests indicate that certain fish products intended for human consumption contain thiaminase which destroys thiamin. They therefore suggest the possibility that certain raw or partially-cooked fish products may prove to be factors in deficiency disease in humans (7).

EXPERIMENTAL DIETARY RESTRICTION, ETC., IN MAN.

Generally speaking, the results of recent studies suggest that too much emphasis has been placed in past experiments on the supplementation of diets, presumably adequate, with vitamins. However, Harrell's work over fairly long periods of time in orphanage children, where 2 mgm. thiamin supplements per child were used, did apparently produce statistically significant improvements in the test tasks compared with the controls (8). "The addition of 2 mgm. of thiamin daily to a fair diet may spell the difference between alert and successful living and a marginal effectiveness" (1).

Vernon and McKinley, treating small groups of senile patients with small and large doses of vitamin B complex, vitamin C and androgens, found on the whole that the results were small and often negligible; moderate doses of vitamins, however, produced in some (mild) cases increased fluency and decreased perseveration (9).

Some interesting experiments have been reported in B-complex restrictions. One, covering a 5-week period in active young men given diets submarginal in thiamin, riboflavin and niacin, produced no significant change in physical or intellectual performance (10).

Archdeacon and Murlin found muscular endurance decreased on a diet low in B complex; inclusion of pure thiamin or pyridoxine (but not riboflavine)

to the diet led to marked improvement in endurance (11). Glickman *et al.* found that the ability of men to withstand the damaging effects of repeated exposures to cooling environments, and to maintain normal neuromuscular and mental efficiency, could be enhanced by giving excessive doses of ascorbic acid, riboflavine and nicotinic acid—in amounts above those required for adequate nutrition (12).

Guetzkow and co-workers found that acute thiamin deficiency precipitated psychoneurotic trends (13). Various aspects of personality were studied in 8 normal young men, maintained 161 days on a partially restricted intake of B complex, when no changes were observed; during a subsequent period of 23 days of acute deficiency significant changes in the psychoneurotic scales—depression, hysteria and hypochondriasis—were found during the use of the Minnesota Multiphasic Personality Inventory; supplementation of the diet by thiamin alone produced rapid recovery (14, 15). Similar personality changes were reported later in further experiments with restricted B complex and protein, reversed by administration of B-complex fractions and protein (16, 17).

Questionable improvement occurred in memory and manual dexterity tests in identical twins receiving thiamin supplements, compared with the control twins receiving placebos (18).

Psychotic patients have been subjected to B-complex restriction, some over long periods. In a group with moderate restriction (400 mcg. thiamin daily and correspondingly small intake of other B-complex factors) changes developed insidiously and late; these consisted of affectual dulling, loss of ambition and interest, and decreased motor activity. Some of a second group receiving only 200 mcg. thiamin daily developed serious emotional disturbances and loss of inhibitory control. In other patients, pre-existing affective trends, such as hypomanic and mildly depressive features, became exaggerated. The formation of paranoid trends was also observed. Among the group moderately deprived of vitamin B complex, the mental changes developed slowly in the course of 3 years. However, among the subjects severely deprived of vitamin B complex, mental disturbances manifested themselves explosively, acutely, or subacutely, after only a few months of depletion. Recovery with a return to the level of pre-experimental behaviour following resumption of vitamin B administration took place in from days to months. It was, in general, rather slow in mildly restricted patients, and dramatic and sudden in severely restricted patients. No claim was made for specific changes, and the affective disturbances noted were based on pre-existing trends (19, 20).

Wet beriberi and other B₁ deficiency states have been produced during the controlled studies at the Elgin State Hospital, but the evidence for the production of syndromes associated with other fractions of the complex is inconclusive (1).

Keys, summarizing some of the more important findings of the Minnesota starvation experiment, stated that subjects losing 10 per cent. or more of their weight showed impairment in endurance and working capacity, which were associated with adverse changes in personality and emotional states. "Starving persons are ordinarily averse to any effort, including that of intellect, and their

preoccupation with food and their own plight may give an impression of stupidity or mental incapacity. . . . Exhaustive studies on memory, reasoning power, verbal and arithmetical facility, and so on, revealed no changes in spite of the subjective impression of most of the men that their mental powers had been reduced." With regard to the personality and emotional changes observed, "externally, the major characteristics are apathy, depression and introversion. Social contacts are avoided and sex interest declines sharply. Psychiatric methods reveal, besides the depression, a well-defined rise in the tendencies to hypochondriasis and hysteria. The behaviour which would ordinarily be associated with increased irritability is suppressed by the overwhelming physical lethargy. It is difficult to appreciate the enormous preoccupation of the starving man with food and eating. His thoughts tend to be exclusively dominated by these concerns. Their expression may range from constant day dreaming about eating to extensions such as interest in scientific agriculture. . . . Even when the food supply is restored, the concern about food persists for many months; a common expression is food hoarding, even when there is not the slightest reasonable basis for this. . . . Personality changes in re-feeding may be even more complex. . . . As the physical state improves, the tendencies towards depression and hypochondriasis diminish. . . . The return of physical vigour allows outward manifestations of formerly suppressed irritability . . ." (21). "Basic intelligence is more resistant to reduction and damage than is intellectual behaviour" (22).

THE SYNTHESIS OF VITAMINS BY BACTERIA IN THE GUT.

As early as 1915 it was suggested that microbial synthesis of vitamins took place in the rumen of the bovine (23). The discovery of the phenomenon of "refection," i.e. the ability of the rat or pigeon to remain unaffected on a vitamin B₁-free diet—so long as the diet contained uncooked starch—was a further step in demonstrating bacterial synthesis in the gut (24, 25, 26). Between 1942 and 1944, with the introduction of the "sterilizing" sulphonamides—sulphaguanidine and succinyl sulphathiazole—it was possible to demonstrate the synthesis of certain vitamins in animals and in man (27 to 32). Najjar and his colleagues used the technique for demonstrating aneurin and riboflavine synthesis, whilst Ellinger and his co-workers in this country found that the same principles were true for nicotinamide (33 to 36). Later, evidence was produced that vitamins may be destroyed by bacterial action in the gut under certain circumstances (37).

The extent of intestinal synthesis (and destruction) of vitamins no doubt varies from individual to individual, and probably varies from time to time in the same individual. According to Ellinger *et al.*, as much as 80 per cent. of the estimated human requirement of nicotinic acid may be manufactured in the gut. The importance of microbial synthesis as a factor in the etiology of vitamin deficiency states has not been clarified, although it has shed light on inconsistencies previously unexplained, and must be taken into account in experimental and other research work involving quantitative dietary vitamin intake.

Many authorities consider that the "type of diet" is of crucial importance with regard to vitamin synthesis by the intestinal flora. Thus certain proteins or amino-acids, by maintaining the "right type" of flora, prevent the development of a nicotinic acid deficiency state, irrespective of the nicotinic acid content of the protein fed (38).

Sterilizing sulphonamides may precipitate a nicotinamide deficiency state, possibly by destruction of the synthesizing action of bacteria. The acute confusional psychosis sometimes noted during the sulphaguanidine treatment of dysentery may have been due to nicotinic acid deficiency. A single case, examined pathologically, showed nerve cell changes consistent with pellagra (39).

It is of interest to note that the sulphonamides were used in infections before their biological significance was understood. "The Woods-Fildes theory that they exert their bacteriostatic action by competition with *p*-amino-benzoic acid, and the later recognition of this substance as a vitamin, either by itself or as a component of pteroylglutamic acid, have now amply justified the classification of these well-known therapeutic agents as antivitamins" (40).

Nicotinamide deficiency has also been reported after oral penicillin administration, and that the latter may act by depressing the microbial synthesis in the gut was suggested by concomitant studies in the nicotinamide methochloride elimination (41).

THE ETIOLOGY OF PELLAGRA.

It was first assumed that a maize diet produced its pellagrogenic effect by its lack of nicotinic acid, since the latter was shown to have a curative effect in the disease. This was doubted (42), and later proved fallacious, since maize diets containing 15 mgm. of nicotinic acid still proved pellagrogenic, whilst other diets containing only 5 mgm. were non-pellagrogenic (43). Krehl *et al.* demonstrated that maize induces a need for nicotinic acid in rats (a species which can synthesize this vitamin), and that tryptophane counteracts this (44 to 47). Gelatin, tyrosine and phenylalanine added to a low protein diet have a pellagrogenic action (48, 49). From these and a number of other animal studies it is clear that the amount of tryptophane in the ration in relation to the intake of other amino-acids is of importance in the etiology of pellagra. Some proteins in maize are deficient in tryptophane.

Krehl and co-workers suggested that tryptophane stimulated nicotinic acid synthesis. Rosen *et al.* (1946) considered that nicotinic acid arose from tryptophane (50). Woolley, however, has pointed out that there was evidence that a toxic substance existed in maize—and with others, that this toxic substance (? indoleacetic acid) was a structural analogue of nicotinic acid (51 to 54).

Experimental pellagra has been produced by large intake of adenine; the latter, or its metabolites, may act by combining with constituents of vitamins or their precursors and thus prevent utilization (55).

These important studies serve to narrow the gap between the previously widely divergent views as to the etiology of pellagra, and to view the factors of nicotinic acid deficiency, protein deficiency and toxic agents in better perspective.

VITAMIN DEFICIENCY STATES IN PRISONERS OF WAR, ETC.

The outstanding recent monographs on vitamin and dietary deficiency states appear to be those of Spillane (1947) and Denny Brown (1947), and both concern studies of malnourished prisoners of war, particularly those in the camps of the Far East (56, 57). Riddoch, in his foreword to Spillane's book, says: "These 'experiments' in nutrition were on a large scale, and it is most fortunate that on the whole the results have been carefully observed and recorded. In P.O.W. camps this was done by medical officers, themselves captive and living with their fellow prisoners in Germany, Burma, Siam, Malaya, Batavia and Hong Kong." Likewise, Denny Brown, in his introduction, states: "The confinement of large groups of men in close captivity in war prison camps, on extremely limited diets for long periods of time, has unwittingly provided data on the effect of dietary insufficiency on a scale that experimental medicine can hardly hope to emulate. Unfortunately, the conditions were seldom such that accurate data as to food values and contents could be plotted against the resulting clinical and pathological effects." Both of these independent works have brought to light certain syndromes related to dietary defect, although the exact relationship between syndrome and syndrome and the precise kind of dietary defect responsible are in doubt. Both authors, in their historical considerations, refer to earlier and classical papers, many of which do mention the existence of some of those syndromes. The monographs bring the latter to the fore, place them in better perspective, and crystallize out the numerous reports of recent observers.

Spillane outlines "the present position concerning the probable deficiencies responsible for the different neurological syndromes of malnutrition" as follows:

Clinical syndrome.	Nature of deficiency.
Pellagra	Nicotinic acid, riboflavin, thiamin.
Beriberi	Thiamin; possibly a second factor in the chronic form.
Acute encephalopathy—Wernicke	Thiamin partly or wholly responsible.
Acute syndrome (Jolliffe)	Nicotinic acid.
Atypical	Unknown.
Retrobulbar neuritis }	? Some factor(s) in the B ₂ complex.
Nerve-deafness	
Sensory ataxia	
Spastic syndrome	Unknown (? deficiency or intoxication).
"Burning feet"	? B ₂ complex (? pantothenic acid).

Denny Brown's list of clinical syndromes tallies very closely with the above, but he adds a myasthenic bulbar syndrome ("Kubisagari"). He considered none of the syndromes were related to beriberi, with the possible exception of the last named. He thought that the burning feet syndrome was allied to acrodynia, and clearly a part of the syndrome of pellagra, although it could occur independently. The syndromes retrobulbar neuritis, spinal ataxia, spastic ataxia and simple spastic paraplegia occurred in various combinations and separately.

He concluded that these represented isolated occurrences of the various neurological manifestations of pellagra.

It is not easy to provide even a rough estimate of the incidence of neuropathies in the various P.O.W. camps. Denny Brown's study concerned 303 clear-cut cases of neurological disorder amongst 3,667 patients received into hospital in the autumn of 1945—these out of 60,000 released British and Indian P.O.W.'s. It must be appreciated that these cases represented survivors, and that reports by medical officers who themselves were prisoners testify a much higher incidence of neuropathy "on the spot." One wonders how many of the 80 per cent. of 60,000 men, who died after being sent to forced labour in Siam, died of B deficiency states (bearing in mind the frequent if not concomitant effect of B deprivation on the myocardium in neuropathy).

Most authors emphasize that beriberi was widespread, and was the commonest deficiency syndrome in most of the camps. Whilst no specific mental changes are referred to in recent papers, Spillane mentions "memory defect," but adds that the latter was not uncommon in unaffected prisoners. Although classical pellagra was uncommon, pellagrous lesions (such as glossitis, scrotal dermatitis and chronic diarrhoea) were frequent. However, in 1940, in Hong Kong, Wilkinson reported 1,000 cases of pellagra with a high death rate (58).

The syndromes about to be presented are described separately, since they existed in "pure form" in some cases. From the literature it appears that a fairly close relationship exists between retrobulbar neuritis, nerve-deafness and spinal ataxia, and, in fact, these conditions are grouped together by Spillane. The position of the burning-feet syndrome is obscure—it occurred independently or in association with other deficiency signs. The spastic syndrome was an independent condition, distinct from the foregoing.

Retrobulbar Neuritis.

"Camp eyes" was one of the commonest, most persistent and disabling affections. It was not confined to camps in the Far East, e.g. Spillane refers to cases from the Middle East. In this condition the majority of cases complained initially of inability to see colours. This was followed by a mistiness obscuring central vision. After 1-3 months the condition improved or remained stationary. Examination of the visual field revealed paracentral scotomata. Many patients complained of dysaesthesiae in the lower limbs, but did not become ataxic.

Spinal Ataxia.

According to Spillane, dysaesthesiae preceded ataxia, as a rule, and retrobulbar neuritis was very commonly present. The dysaesthesia appears to have been, in some cases, identical with the "burning-feet" syndrome. Ataxic symptoms developed over a period of weeks or months. Loss of vibration sense, hypoaesthesia and hypoaesthesia spreading up to the waist line and gross disturbances in hot and cold sensations were objective findings, with usually exaggerated tendon reflexes in the lower limbs, but with absent reflexes in a few advanced cases.

Tinnitus and Deafness.

Tinnitus was sometimes complained of at the time of onset of visual loss, and deafness of central type gradually ensued in a few cases.

Laryngeal Paralysis.

A weak and hoarse voice noted in a few patients was due to partial abductor paralysis of the vocal cords.

Mental Status Associated with Retrobulbar Neuritis—Ataxic Syndromes.

According to Spillane, many complained of failing memory, especially for recent events. Many were apathetic, some mildly depressed. The memory defect appeared not to be significant in the majority, but in a few was severe and pathological. One patient with severe ataxy exhibited some degree of intellectual impairment, whilst another developed hallucinations and delusions of persecution. Denny Brown also confirms that a few patients with the ataxic syndromes presented "slowing of mental function," one being markedly apathetic and another disoriented and confused.

Spastic Syndrome.

This uncommon syndrome appears to have been clearcut and distinct from the group described. In Spillane's 7 cases, 3 gave a history indicative of cerebral disturbance at the outset, and had probably passed through an initial confusional episode. These cases, 3 years after onset, exhibited varying degrees of spasticity of the lower limbs, unaffected arms, and normal sensation. Rigidity varied, but some cases were bedridden. Tendon reflexes in the lower limbs were exaggerated, and plantar responses extensor. Denny Brown's 9 cases presented a similar picture, but he mentions a spastic speech and expressionless facies; 3 of his cases at the onset of the illness had been mentally confused—but when examined by him the mental state was normal.

Graves (1946) studied 37 cases at first hand and in the initial stages (59). The illness began with difficulty in walking, and pains in the legs and spine. Later mental dulling, diplopia and spasticity appeared. Six patients died, having presented an acute organic syndrome which included "restlessness, confusion, incontinence, diarrhoea, gross rigidity, and sometimes maniacal outbursts." A further 6 cases recovered after having passed through an acute delirious episode. Residual signs of this syndrome consisted of spastic difficulty in walking in half the cases, amblyopia (40 per cent.), mental changes (41 per cent.), "burning feet" (38 per cent.), paraesthesiae (7 per cent.), pain in the spine (6 per cent.), and diplopia (5 per cent.). Epileptiform seizures were reported in the acute stages in 2 cases. In one case athetoid movements and tremors, reminiscent of "typhoid pellagra," characterized the confused period.

In differentiating the spastic syndrome from the polyneuritic and sensory ataxic groups, Spillane refers to the absence of muscular wasting in the former, and absence of sensory loss in the latter.

"*Burning Feet.*" ("Jittery Legs," "Happy Feet," "Electric Foot.")

A common and distressing syndrome in some P.O.W. camps, affected thousands of men and consisted of severe burning sensation over the soles of the feet, especially over the region of the heads of the metatarsus, with redness, slight swelling, hyperalgesia and sweating of the part (60, 61). The pains were severe at night, disturbing sleep so much that the sufferer often paced restlessly in the endeavour to relieve suffering, or "men sat day and night soaking their feet in cold water and rubbing their own and each others' feet for relief" (62). These emaciated patients were reported as despondent, and some showed memory disturbances. Katz refers to the lack of morale, indifference to body cleanliness, irritability, negativism, and variable degrees of impaired intellectual function (63). Peraita described this as the most frequent syndrome observed in Madrid during the Spanish Civil War (64).

Myasthenic Syndrome.

Musselman briefly mentioned a syndrome somewhat similar to myasthenia gravis which occurred in epidemic proportions following an epidemic of dengue, 30 per cent. of 500 men in one camp being so affected (62). It was characterized by a tiring of the eyes, diplopia, ptosis, weakness of the neck and face, and difficulties in talking and swallowing. Katz described the condition in the same group of patients in more detail (63). Graves also observed 3 patients who developed a similar syndrome—drooping of the eyelids from midday onwards, with complete relief next morning, fleeting diplopia and inability to hold the head up in the evening; bilateral ptosis was a constant sign.

Nicotinic Acid Deficiency Encephalopathy.

Although no papers were published under this heading, and Denny Brown only refers to the condition as a possible, though unlikely, explanation of the cerebral symptoms in the "spastic syndrome," Spillane believed that a number of such cases occurred in his Channel Isles series (65). He admitted that in treatment, B complex was administered, so that it was impossible to ascertain the relative importance of riboflavin, nicotinic acid and thiamin in the production of the clinical states. He described patients with hunger oedema, with profuse diarrhoea, rapid pulse, distended abdomen with periodic visible peristalsis. Restlessness, delirium and confusion were the main mental features. The patients' mouths were often filthy, ulcerated, and the tongues raw and reddened. After glucose saline drips some patients showed a change in behaviour, with grimacing and shouting, whilst tetanic spasms and rigidities were added to a picture which sometimes heralded a fatal ending. Those patients recovering were disoriented, confused and amnesic for two weeks or so, followed by transient lucid intervals. Spillane noticed that months later some patients were still confined to bed in a listless state, with slight or moderate memory defects and exhibiting neuritic signs.

In his chapter on nicotinic acid encephalopathy, Spillane also refers to "indigent Arabs in the Middle East who were admitted to hospital on being

picked up in the street in an unconscious state, responding dramatically to intravenous nicotinic acid. They were invariably malnourished, often emaciated, with chronic diarrhoea, infestation, anaemia, and the chronic skin changes of nicotinic acid deficiency. Stupor was almost invariably accompanied by restlessness, tetanic spasms of the body, and tremors and rigidities of the limbs. Grasping and groping movements sometimes continued for hours at a time, and the lips and tongue writhed and twisted, the patient sometimes emitting smacking and loud sucking sounds. The slightest tap on tendon or muscle would elicit tremor, fibrillation or clonus, and evidence of changes in the peripheral nerves and spinal cord was very common. Glossitis was also common"

Musselman reported delirium as frequent in cases of deficiency disease when acute infections such as malaria or dysentery occurred. He referred to a hypoglycaemic syndrome at a period when rations were extremely reduced—patients becoming excited, hyperpnoeic and exhibiting hysterical reactions. Nicotinic acid and thiamin relieved "cerebral symptoms" (62).

Wilkinson, in his report on the outbreak of pellagra in Hong Kong, noted no organic nervous signs in the early stages, but nervous symptoms such as headaches and insomnia were prominent (58). Twenty-one cases were delirious, 4 became maniacal. Commenting on treatment, the author stated, "few things in medicine are more dramatic than the effect of nicotinamide given intravenously in acute pellagra; a patient, who on admission is feverish, disoriented, rambling in speech, unable to co-operate or swallow, will in 72 hours be rational, hungry and able to swallow."

Wernicke's Encephalopathy.

An admirable summary of modern conceptions of this syndrome is included in a special chapter in Spillane's book. The brief remarks here draw attention to what appear the most important recent advances, particularly from the clinical aspect.

Although not common, it is probable that the syndrome may be overlooked and not diagnosed. Chronic alcoholism is not the sole basic etiological factor, for it occurs in association with pernicious anaemia, persistent vomiting, pregnancy and hyperemesis, in the terminal stages of carcinoma of the stomach, and sometimes in depressive psychoses.

Riggs and Boles studied 42 cases which had occurred at the Philadelphia General Hospital over a 10-year period, and found a history of chronic alcoholism in only 18 cases (66). Sixteen patients gave a history of prolonged vomiting prior to the onset. Thirty-four cases showed severe hepatic damage at necropsy. There were 9 cases of malignant or degenerative lesions of the digestive system. Twenty-three had acute infections. The general conclusion of these authors was that the clinical syndrome as originally described by Wernicke was of little value in diagnosis. The classical triad of clouding of consciousness, ophthalmoplegia and ataxia was only noted in its entirety in one patient. Furthermore, findings which are regarded as manifestations of the condition frequently occur only in the agonal period. From the pathological aspect lesions were by no means confined to the classical sites, but affected such

regions as the dorsomedial nucleus of the thalamus and the inferior olives, and were often associated with widespread chronic degenerative changes throughout the brain.

Meyer investigated pathologically 7 cases of the Wernicke syndrome. In 2 there was a history of alcoholism, in 3 pernicious anaemia, one followed hyperemesis gravidarum, and the other followed gastric carcinoma. The latter case was discussed fully, and was distinguished by an atypical clinical course in which mania had been present for a considerable time. The oldest and severest lesions were in the anterior portion of the hypothalamus. Meyer tentatively suggested that it was "conceivable that subtle and reversible abnormalities underlie functional mania, and that they are localized in the same cerebral system which is the site of histological lesions in certain organic cases displaying manic symptoms" (67).

In the Wernicke syndrome Hess points out that certain "vegetative" signs are characteristic, e.g. lethargy, pupillary changes, tachycardia, irregularities of respiration, the vomiting and dizziness at the onset. These are dependent on the site of the anatomical lesions (68).

Spillane states that the present clinical conception of the syndrome will have to be enlarged, although he is unable to suggest any clearcut clinical picture. Some guidance, however, has appeared from the observations of de Wardener and Lennox, who were able to recognize the nature of the illness at an earlier stage in a P.O.W. camp, owing to the epidemic character of the outbreak (69). These authors stress certain mental symptoms, disturbances of vision, loss of appetite and vomiting in the earlier stages of the disease. Nystagmus was the earliest sign, and occurred invariably at the outset (although it disappeared in the later stages if ophthalmoplegia developed). Weakness of the external recti occurred in about a quarter of the cases, but other eye signs were uncommon. The mental symptoms consisted of apprehension and anxiety in the earlier stages, followed by increasing depression and emotional instability. Loss of memory for recent events was noteworthy. Later, with the onset of confusion, disorientation in time and place occurred, and "mild confabulation and hallucinations occasionally preceded the onset of coma." The authors mentioned that this progression of symptoms was not invariable, and that excitement or hallucinosis occurred occasionally as early symptoms, heralding a rapid onset of coma. De Wardener and Lennox considered Wernicke's encephalopathy to be produced only by an *acute* thiamin deficiency, as compared with beriberi, where the condition is subacute and less severe.

In a recent report on the Wernicke syndrome Barrie found 3 cases out of 3,000 necropsies coming within the surgeon's province. The first case may have developed gastric atony and vomiting from a diet grossly deficient over a prolonged period in B₁; the second case, who had sufficient B₁ in the diet, developed pyloric stenosis and habitual vomiting, which brought about starvation; the third case was one of vomiting associated with carcinoma of the stomach (70).

Kravitz and Stockfisch reported 3 cases said to be due to dietary defect, who showed gross oculomotor lesions, recovering with B₁ administration (71). Hardwick reported 3 confused patients, 2 of whom exhibited signs of peripheral

neuritis, who responded well to vitamin therapy. Nystagmus was not noted, but 2 cases had signs suggesting midbrain involvement (72).

Considerations with Regard to Etiology and Inter-relationship of the Above Syndromes.

In his scholarly review and criticism, Denny Brown doubts if retrobulbar neuritis or ataxia are related to beriberi, i.e. produced by the same causative factor (57). He doubts the relationship of the ataxia occurring in the Wernicke syndrome to thiamin deficiency, and points out that retrobulbar neuritis, ataxia and deafness are not regularly observed to precede cases of Wernicke syndrome. He points out that these syndromes have been reported prior to the last war in various papers, either in association, or independently. Peraita, in his reports concerning the Spanish Civil War, referred to similar conditions. The cases of Wilkinson, and of Wilkinson and King approximated closely to those of classical pellagra, and the cord symptoms were of spastic type; these authors found that the response of amblyopia, often associated with mucocutaneous lesions, to nicotinic acid or riboflavin was spectacular (58, 73). Garland also pointed out that in his cases (which exhibited defects of vision, hearing and gait) he was able to analyse carefully the dietary, and he concluded the nicotinic acid content was doubtfully sufficient (74). On the other hand, Whiteacre and Adolph *et al.* found thiamin and nicotinic acid less effective, although the administration of yeast led to slow improvement (75, 76). Spillane, and Scott and Spillane, found good results with liver, or liver extracts (77, 78). Butler *et al.*, in their rapid nutritional survey of American civil internees from Japanese camps, found many cases of impairment of vision and a few with central scotomata 4 months after receiving adequate dietary; peripheral neuritis was frequently co-existent (79). Clarke and Sneddon reported similar findings, but their conclusion was that a toxic agent or an unknown antivitamin factor in spoiled rice played a part (80).

Summarizing, Denny Brown states that there was a widespread incidence of these syndromes in areas on "marginal diets largely composed of cereals." The proportion of retrobulbar neuritis, ataxia and spastic symptoms differed from one group to another. The association of frank beriberi with such cases varied, being highest in the cases reported by Clarke and Sneddon. Wide discrepancies were observed concerning the etiology, from specific deficiency of one vitamin of the B complex, to toxic agents and antivitamin factors. Denny Brown agreed with Stannus, in the main, that all these syndromes were closely associated with pellagra.

Shah postulated that avitaminosis played a part in lathyrism (81). The similarity between the spastic syndrome and lathyrism has been closely observed by Denny Brown and Spillane. Thus, the former noted that the only purely spastic syndromes regularly associated with dietary fault are lathyrism and ergotism. Discussing the clinical aspects of lathyrism, Denny Brown points out that there is usually no sensory loss, no clouding of consciousness nor epilepsy. A degree of recovery occurs after a single attack, but spastic extension of the legs, pes cavus, over-adduction of legs and scissor gait are common sequelae. There was no suggestive evidence from the cases

observed in P.O.W. camps that grain had been contaminated by vetch or chick-peas, and if some toxic antivitamin substance had been responsible in the dietary it was very inconstant. Spillane further observes that cerebral symptoms are not usually described in clinical lathyrism.

Denny Brown considers the "burning-feet" syndrome to be closely related to acrodynia and pink disease in children. He concluded that there was good evidence that this syndrome, with or without corneal degeneration, was a separate entity associated with an exclusively cereal diet. He further suggested that the "*causalgie nocturne spontanée des vieillards*"—a fairly common syndrome in temperate climes—was not an uncommon related syndrome.

The causative factors in the myasthenic syndrome appeared obscure. Musselman's report suggested that a dried-fish diet was in some way responsible, but not all the patients consumed this diet. Graves reported that his cases had consumed large quantities of tapioca and thus unbalanced the diet. The theory that thiamin deficiency, resulting in over-rapid destruction of acetylcholine, explains the phenomenon does not hold water, since, if this were the case, the myasthenic syndrome would be commonplace in thiamin deficiency, which is not so. (The relationship between acetylcholine formation and thiamin, however, is probably close) (82).

Lesions produced in the C.N.S., experimentally in animals, are only of partial help in our understanding of the mechanism occurring in humans. Thus, Wintrobe and his co-workers have been unable to produce polyneuritis in swine by vitamin-deficient diets (83). Controversy still exists with regard to the relationship of polyneuritis occurring in man and thiamin deficiency as the sole etiological factor (84). On the other hand, the effects of acute thiamin deficiency in animals point to a disorder of the righting reflexes and a disorder of the functions of the brain stem which correlate fairly closely with the effects observed and recorded in humans. Such symptoms are readily reversible (85, 86). Swank has shown that gradual deprivation of thiamin leads to polyneuritis, and that the largest and longest nerve fibres were found to degenerate first (87). His further observations have their correlates in human beriberi. Acute riboflavin deficiency in dogs produces a characteristic syndrome with sudden death, and chronic partial deficiency produces the gradual development of ataxia with degenerative changes in the peripheral nerves, dorsal nerve roots and dorsal columns of the spinal cord (88). Despite the contention of some, the precise influence of riboflavin deficiency in the etiology of syndromes in man is unknown (89). It appears very doubtful if any degenerative lesion of the nervous system can be attributed directly to nicotinic acid deficiency.

Denny Brown pointed out that the spinal ataxia of nutritional deprivation was different from the dorsal root ataxia in pantothenic acid and pyridoxine deficiency in swine, since some human cases did not show loss of tendon reflexes (suggesting that the lesion was not primarily ganglionic). In a later paper the same author reports 2 human cases who suffered from bronchogenic pulmonary carcinoma, who exhibited primary simple degeneration of the dorsal root ganglion cells (associated also with a primary degenerative condition of muscles) (90). The relationship with regard to specific deficiency factors

compared with Wintrobe's ataxia in swine is presumably close, and it was postulated that bronchogenic carcinoma might produce a by-product (? analogous to thiopanic acid, or phenyl pantothenone) which interferes with the biological conjugation of pantothenic acid in metabolism.

The cerebral symptoms observed in the spastic syndrome must have a different etiological basis from the Wernicke syndrome, since the latter is not associated with spastic disorder, and nystagmus was not a feature of the spastic disorder.

Hibbs, unlike the majority of observers, thought that the "burning-feet" syndrome was a phase in the progressive development of beriberi (91). Although Smith found nearly 80 per cent. of his series of the "burning-feet" syndrome to have evidence of nicotinic acid or riboflavin deficiency, it is probable that pyridoxine and pantothenate are more closely related (92). Gopalan investigated 53 cases and found marmite and calcium pantothenate injection relieved symptoms, whereas thiamin, nicotinic acid and riboflavin were ineffective (93).

With regard to the myasthenic bulbar syndrome, Denny Brown suggests a deficiency in some essential, e.g. tryptophane. Spillane, on the other hand, thought the condition might have been a variant of the Wernicke syndrome—and he points to the clinical features and the response to thiamin.

Conclusions.

Although many attempts were made to relate the qualitative and quantitative aspects of the dietary to the syndromes observed, so many other factors were clearly involved that no substantial addition to knowledge was gained in this direction. Thus, Denny Brown states, "the content of any given diet, in known vitamins, is far from being an accurate indication of the mechanism of nutritional lesions." The possibility of toxic factors, e.g. poisonous alkaloids, was put forward in some instances, but appeared unconvincing when conditions between camp and camp were considered. Starvation and vitamin deficiency are quite distinct—hundreds of cases of starvation without deficiency occurred in Germany (94). Probably the following were important causative factors: the relative high carbohydrate and low protein diet (examples were noted of the effect of sudden unbalance of dietary by extra carbohydrate rations); the quality of the protein and its tryptophane content.

Recent studies of experimental deficiencies in animals (*vide supra*) have not materially helped in elucidating the mechanism in human cases. Thus, there is no convincing proof that riboflavin, pyridoxine or pantothenic acid deficiencies are related to the retrobulbar neuritis—deafness—ataxic syndrome, the spastic and the myasthenic syndrome.

Factors which stand out as being important are those concerned with infection—particularly of the gastro-intestinal tract. Dysenteric and other infections were rife and widespread in P.O.W. camps. Although diarrhoea is a common and early symptom of pellagra, and may precede other signs of the disease by long periods, undoubtedly chronic diarrhoea itself is an important agent in the production of nutritional disturbance in the C.N.S. Toxaemic processes may produce effects in the presence of nutritional deficiency which do not arise when nutrition is normal. It was frequently noted that

acute dysentery and other infections precipitated or caused a relapse of deficiency syndromes.

Wilkinson reported that all the pellagrins he tested showed achlorhydria, and accepted this as an important factor explaining why still more cases did not develop the disease in Hong Kong.

The effect of forced, excessive exercise in poorly nourished subjects may well have been a further important factor—as suggested by McLardy (95).

In general the evidence from therapeutic effects reported in the various syndromes is conflicting, and has led to no clear-cut conception of specific factors being invariably involved. Moreover, vitamin B treatment was applied promptly and energetically on some occasions in the syndromes mentioned, and the results by no means prompt and successful. Although it must be conceded that other and perhaps unknown factors are operative, one must bear in mind the conception of “biochemical lesion” and “morphological lesion”—“it does not necessarily follow that the failure of vitamin therapy to reverse a pathological process means that the disease is unrelated to deficiency of the vitamins.” Thus, Spillane suggests that perhaps weeks before the onset of visual defect the subject was grossly deficient in B factors. It would be of advantage, therefore, to have some conception of the minimal and earliest symptoms and signs of B-complex deficiency states. Unfortunately, this has proved difficult in the absence of simple, reliable and rapid biochemical tests, and the clinical diagnosis of mild B deficiency in an isolated case is wellnigh impossible.

Russell Brain points out that we know next to nothing about the needs of the C.N.S. for proteins and amino acids, although glutamic acid may prove important in cerebral metabolism. Vegetables manufacture the thiamin and nicotinic acid which man consumes, either directly or indirectly, although the intestinal microbial synthesis is an additional source of supply. Brain agrees with Walshe that the polyneuritis in beriberi is caused by an intoxication with pyruvic acid and/or allied intermediate products of sugar metabolism, which is incomplete owing to lack of thiamin. The latter may do no more than to put an end to the intoxication of a perverted sugar metabolism. With regard to the etiology of Wernicke syndrome, Brain questions individual susceptibility and other factors such as rate of onset, influenced by dysentery and diarrhoea. He is sceptical about Denny Brown's conclusion that the syndromes described above may be considered pellagroid. In his opinion the addition to our knowledge as a result of war experience is disappointingly small (96, 97).

Deficiency Syndromes in the Spanish Civil War (1936-39).

The pattern of deficiency states reported by Peraita and others resembled to some extent those observed during World War II. The main groups were : (a) pellagrous states, (b) paraesthetic and causalgic conditions, (c) retrobulbar neuritis, (d) neuritis of the auditory nerves, and (e) simple glossitis. Hunger and famine oedema was also common.

Subsequently patients complained of weakness, forgetfulness and irritability. Some became depressed. Insomnia and disturbed sleep rhythm were frequent.

In more severe cases consciousness was clouded, confusion and states of stupor occurred. Some patients apparently showed signs of intellectual deterioration.

Summarizing his experience, Peraita divided some 300 patients observed into three groups—one third showing psychological symptoms, one third exhibiting pellagrous skin lesions together with neurological disorders, and the other third showing similar neurological changes without cutaneous lesions (56, 64).

MISCELLANEOUS.

Pernicious Anaemia, Folic Acid and Vitamin B₁₂.

Ferraro *et al.* examined the cerebral changes in 7 cases of P.A. : in 5 P.A. had developed in psychotics, in 1 case of P.A. a psychosis followed, whilst the seventh presented no neuropsychiatric signs. The vascular changes in 2 cases were of maximum intensity in the regions specifically affected in Wernicke's disease, and the authors regarded these cases as abortive forms of that condition. Since 4 of the 5 psychotic patients suffered from a paranoid condition, the authors suggested that there might be a common constitutional factor (98).

The significance of folic acid (pteroylglutamic acid) in relation to psychiatric problems is at present obscure. An enormous volume of research has recently been conducted on this substance. The suggestion that it may function as a metabolic antagonist for glutamic acid and competitively interfere with the nutrition of the spinal cord has been put forward without experimental or other evidence (99, 100).

Davidson and Girdwood reported that 4 patients with megaloblastic anaemia treated with folic acid developed the clinical features of peripheral neuritis. Another case with sprue developed a pellagrous syndrome with folic acid. The mechanism may have been vitamin imbalance. The authors suggested that purified liver extract may contain a factor which liberates various members of the B complex from inactive forms, or possibly facilitates their absorption or utilization (101).

Although folic acid was found to transform megaloblastic to normoblastic haemopoiesis, the improvement was not always maintained, and C.N.S. lesions present were found sometimes to deteriorate with treatment (102). During 1948 a very potent compound of high anti-anaemic activity, crystallizing in the form of small red needles, was extracted from liver (103, 104). The suggested designation of vitamin B₁₂ seems to have been universally accepted. Not only does B₁₂ restore the blood picture, but several reports testify that lesions in the C.N.S. may be arrested, or even improved (99, 105, 106). It is not yet certain that B₁₂ is the anti-anaemic liver principle, although some authorities go so far as to suggest that the so-called extrinsic factor might be identical with, or closely related to, B₁₂ (107). The discovery is of psychiatric import, since psychoses may be associated with P.A., based on organic lesions. Although Adams and Kubik concluded that "patients with brain lesions have mental symptoms and that the converse is not always true," the possibility of "biochemical lesions" must be borne in mind (108).

Neurosis and Vitamin Deficiency.

Clarke and Prescott reported 17 cases of deficiency of B complex associated with oral lesions and mental symptoms. The "marginal war-time diet" was a common factor, but other important factors were evident in these cases, e.g. the strict adherence to "special diets," e.g. in peptic ulcer and obesity, and conditions interfering with absorption such as vomiting and gastrointestinal disease. They noted in their cases "the invariable presence of symptoms usually regarded as psychoneurotic, but which cleared up with vitamin B therapy without alteration in the environment or special psychological treatment" (109).

Leitner, in his review, stresses the similarity between the symptoms of "neurasthenia" and early vitamin deficiency (110). Weir Mitchell's properly balanced forced diet plus rest, and the modern version, modified insulin, are often effective in treatment of certain neurotic states. Leitner raises the question of possible importance of deficiency factors in the etiology of neurotic symptoms. He further stresses the need for detailed attention to the dietary history in psychoneurotics.

Vitamin Deficiency in the Aged.

Meyersburg reported pellagra occurring in the senium, and states that senile psychosis may be simulated by pellagrous encephalopathy in the aged (111). Robinson, Wadsworth *et al.* and Gillespie had in previous papers warned clinicians of the possibility of deficiency syndromes in old people, particularly perhaps those exhibiting delirium and confusional states (112, 113, 114).

McNeely and Jones report a case of secondary pellagra "caused by multiple argentaffin carcinoma of the ileum and jejunum." Although the mechanism may have been faulty absorption of nicotinamide in the gut, the case was complicated, since secondary deposits were present in the liver also (115).

Recently, Rafsky and Newman have described a relative thiamin deficiency in aged people on diets which are qualitatively adequate for young adults (116). They concluded that diets for some aged people needed enrichment. Mills's work on the requirements of ageing rats appears to support this, for he found an increasing thiamin requirement with advancing age, although there was not a corresponding increase in demand for other factors of the B complex studied (117).

Deficiency Factors in "Toxic-Exhaustive Psychoses."

Foster reviewed 40 patients, admitted over a period of a year to hospital, suffering from a "toxic psychosis" (118). He concluded that toxic psychosis on a nutritional basis may occur without physical signs of vitamin deficiency. If nicotinamide therapy is commenced immediately after the onset of the psychosis, and adequate diet restored, the response is often rapid and dramatic. If the history is longer, response to nicotinamide is slower and will not occur until normal liver metabolism is restored—and this may take some months.

If the latter is effected, patients recover without exhibition of massive doses of nicotinamide. The author found liver insufficiency in all long-standing cases in this group, and stated that improvement in the mental state could not be effected until this was corrected. E.C.T. was of no value in such cases, and insulin shock was contra-indicated. Vitamins alone in severe cases were also of no value. The author would substitute "nutritional psychosis" for the term "toxic psychosis."

Tongue Lesions in Deficiency States.

Tongue lesions occur in vitamin B deficiency states, and have been described in association with nicotinamide, riboflavin, pyridoxine and biotin (119). It is reported that such lesions can be detected at an early stage in inspecting the tongue under ultra-violet irradiation screened with Wood's glass. Whilst the defective fluorescence observed may prove a clinical aid to the early diagnosis of certain deficiency states, caution is needed at present, since complex problems are involved and the work is as yet in the experimental stage.

Toxic Effects of Vitamin B₁.

Leitner reports untoward effects with large doses of vitamin B₁. In one case a condition resembling anaphylactic shock with eosinophilia resulted; in another the symptoms resembled those of thyroid overdosage (120).

Toxamins and Antivitamins.

Some foodstuffs contain substances which interfere with the action of vitamins. Phytic acid has rachitogenic effects, dicoumarol opposes vitamin K, avidin opposes biotin, certain substances in maize nicotinic acid. According to Kodicek, "toxamins" interfere with the action of vitamins, whilst anti-vitamins are chemically analogous substances to vitamins. The significance of the above is that it adds to the perplexities of the analyst called upon to estimate the vitamin values of food (121).

Deficiency and C.N.S. Infection

Symonds, in an interesting short article covering a wide field, in which many points of considerable interest to psychiatrists were referred to, quotes Bodian, who produced pyridoxine deficiency in a rhesus monkey by the administration of the specific antivitamin, desoxypyridoxine; the animal developed poliomyelitis (104). The author considered, from the evidence of his experiments, that B₆ deficiency had deprived the animal of its natural immunity to the virus when given by the mouth. This suggests that specific vitamin deficiencies may be related to susceptibility to virus or bacterial infection.

Wilson's Disease.

Uzman and Denny Brown have recently found a severe and persistent aminoaciduria in cases of hepato-lenticular degeneration (Wilson's disease) (122). In one of the cases reported, where the liver was presumably severely

damaged, the patient exhibited marked neurological and mental disturbance. The question arises as to whether there is not a fundamental basic defect in the metabolism of amino-acids in Wilson's disease, so that by their absence the maintenance of the functional integrity of the liver and basal ganglia of the brain is impaired.

Agene.

In 1946 Mellanby reported that hysteria in dogs could be produced by feeding them on flour treated with agene (nitrogen trichloride), the flour improver and bleacher in common use for the past 25 years in Britain (123). Similar symptoms were found to occur in cats, rabbits and ferrets, but exacting tests revealed no definite evidence of harm being produced in man. Nevertheless, the U.S. Government has now prohibited the use of agene as a flour improver and its use is being discontinued in Great Britain also. Recently, a crystalline toxic factor associated with the protein fraction of flour has been isolated (124).

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PHYSIOLOGICAL PSYCHOLOGY.

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GENERAL.

It must be admitted that physiological psychology has up to now hardly justified its claim to constitute a separate discipline in the study of human psychology. Much that has been included under this term is a description of anatomical dispositions that might account for certain behavioural entities, but which lack at present any experimental physiological justification.

The past five years have seen an attempt to reformulate the basic conceptions of physiological psychology in terms of neural mechanics. This theoretical approach, for it cannot be claimed that it is as yet on an experimental basis, promises to exercise an influence on the study of the physiological concomitants of mental activity as revolutionary as the mental mechanisms of the psychoanalytic school had on descriptive psychology. This new discipline for the study of neuronic intercommunication and the resulting co-ordination of nervous and mental activities has been given the name of Cybernetics, and, as may be inferred from the derivation from κυβερνήτης—a steersman—the principle involved is that of autoregulation. The neuronic system envisaged by cybernetics is not only self-regulative and goal-seeking but self-correcting.

Ashby (1949) instances an instructive example of such a goal-seeking and potentially self-regulating mechanism in the radar-controlled searchlight. In such a system the light emits a beam of pulses and, guided by the returning reflections, endlessly scans the sky in the absence of any aircraft, but turns towards any reflecting object; and thus when once illuminated the aircraft is held continuously in the beam in spite of all manoeuvres. Such a goal-seeking system must, to be effective, obviously require what is not very happily called a "feedback," that is, a return or afferent impulse from the effector organ. The evidence of the existence of such a return or feedback system has long been recognized by neurologists in any behavioural unit without, however, any very clear appreciation of its importance in determining the goal-seeking or teleological character of the mode of activity. It is largely due to Wiener (1949) that it is now recognized that the action of such a feedback system on a stable nerve mechanism admits of mathematical expression, and that from such mathematical analysis prediction of activity in response to a new determined situation is possible. It must not, however, be assumed as self-evident that, even when dealing with comparatively simple and restricted forms of activity, the mechanisms postulated in cybernetics necessarily participate as the dominant factors. At the most it can be claimed that some such scheme furnishes a possible groundwork for many forms of nervous activity, and hence must, if adopted, prove to be the basic structure of physio-

logical psychology. Even in the simplest activities we have irrefutable evidence of other sources governing activity, other than those envisaged by the cyberneticist, in what we know of the functional significance of the various hormonal, biochemical and catalytic factors. These factors play an often very considerable or even predominant role, increasing in importance with the relative complexity of the biological reaction under consideration. However readily we may adopt a cybernetic formulation for a spinal reflex—and even here we cannot ignore the formation and distinction of excitatory and inhibitory substances—it is quite certain that the physiological psychology of mating is, in the main, governed by hormonal and biochemical drives that outweigh in importance the possible neuro-electronic concomitants. These and similar facts, founded as they are on biochemical and endocrinological evidence, must ultimately be integrated in the physiologists' scheme, and to neglect them in an account of biological activity is to incur all the errors and fallacies of oversimplification. That the logical processes implied by mathematical thought can be practically carried out by a mechanism of the nature that we are considering, that such a mechanism can be goal-seeking and capable of self-correction, that it may memorize or at will expunge its memories, all this has been made most admirably clear by W. R. Ashby (1948) and illustrated by his model "homeostat," but in his guarded account he is careful to claim nothing more. If the electronic model is to furnish the basis of physiological psychology it must be supported by empirical evidence; it is not in the province of physiological science to adopt hypotheses after the fashion of Vaihinger's philosophy of the "als ob (as if)".

Turning to experimental physiology we have, in the study of simple reflexes, direct evidence of the principle of the goal-seeking mechanisms with self-correcting negative feedback, and possibly nowhere is this better exemplified than in the "Abwisch reflex" of Pflüger's spinal frog, though even at this level a holistic survey of the integrated reflex reveals the inadequacy of an account that leaves out the biochemical storage and destruction of guiding forces in the environment. Much play has been made by opponents of this new physiological psychology on the utterances of Jefferson (1949) in his Lister Oration. Jefferson rightly points out that in its present form the electronic model cannot be said to have thrown any light on axiology or on conscious emotion, but this objection arises from a misconception of the limitations imposed by any scientific account of nervous activity. The omissions to which he draws attention belong to another universe of discourse; it makes no sense to ask the physiologist to give an account of this in terms of mechanism, and it is equally impossible either to predict or to deny its eventual applicability; Robert Watson-Watt (1949), as a physicist, has emphasized this point in his essay on "Electronics and Free Will." As to any further evidence obtainable from the study of electroencephalography, though there is much that is apparently compatible with the cybernetic hypothesis, the conditions are too complicated to admit of anything compelling proof of its validity. That the alpha activity of the area of visual integration is modified concomitantly with psychological events should furnish a basis for an expression of such activity in terms of physiological psychology, but as yet we can get little

further than the elaboration of schemata which, if not mutually contradictory, are at this stage difficult to correlate one with another.

To quote an admirable concise survey of the question by the Walters (1949), "Whilst Adrian assumes that the regular sinusoidal alpha rhythm is due to an as yet unexplained synchronization of groups of cortical neurones, and that the breaking up of the rhythm is due to the irregular intensification of the activity of these cells by unsynchronized centrifugal impulses, Bremer (1947) believes that the resting rhythms are expressions of an incessant alternation of excitation and inhibition, reminiscent of the "hunting" exhibited by a crude servo device. McCullough (1947), Pitts (1947) and Walter (1947) suggest that these rhythms have a more subtle function—that of scanning the projection areas for information. The presence of several components in the alpha rhythm suggests the possibility of interlaced scanning, possibly connected with such psychological functions as recognition and recall. The blocking reaction is inevitable in such a system. The scanning sweep is supposed to be stopped when it encounters a region of activity. Darrow (1940, 1947) regards the alpha rhythms from an entirely different view-point; he considers it to be a cause rather than a consequence of repose. He describes the cortico-thalamic feedback pathway as a governor or escapement system whereby cortical activity is limited to a burst of activity every half cycle. G. L. Freeman (1948) summarizes this particular line of approach to the understanding of the energetics of human behaviour in the following words: "All behaviour is an attempt to preserve organismal integrity by homeostatic restoration of equilibrium."

An alternative approach to the problems of physiological psychology is provided by the general biodynamic theory of behaviour of Masserman (1946). This theory is as yet descriptive rather than explanatory. The holistic approach that Masserman describes demands the integration of physiological and psychological accounts of behaviour. It is essentially experimental, as in his pioneer work on artificial neurosis, but because of the experimental approach, control observations are possible, and whether or not psychological deductions are directly admissible, light is thrown on the organic basis of behaviour.

CEREBRAL CORTEX.

Additions to our knowledge of the functions of the cerebral cortex in its relation to psychological activity, other than those due to electroencephalography, depend often on inferential conclusions based on anatomy. A general review of electroencephalography appears elsewhere in this volume. A brief account of the recent work on sensory representation in the cerebral cortex appears in the symposium on functional organization of the cerebral cortex organized by the American Physiological Society, 1947. Woolsey (1949) reports on the sensory areas. The work from the Physiological Laboratory of the Johns Hopkins has established that each of the principal afferent systems has a double representation in the cortex. Thus touch, sight and hearing are represented in two separate areas in each hemisphere. When spontaneous cerebral activity has been reduced to a minimum by profound

barbituric anaesthesia, stimulation of the receptor organs permits the definition of the primary cortical area involved, whilst the intra-cortical synapses are blocked. Though the application of these observations to physiological psychology may as yet be indirect, they may, if verified for the human brain, provide the basis for certain imperfectly understood functional replacement processes after limited cortical destruction. Marion Hines, in the same symposium, gives an account of motor localization in the primates that similarly supplies the physiological basis for the two distinct types of volitional movement. The idiokinetic system serving local and precise motor activity linked even to single muscles, together with its respective suppressor mechanism, is situated in the posterior portion of area 4, whilst the more anterior holokinetic system is concerned with the coarser postural and whole limb movements. In the foetal macaque the idiokinetic territory which develops later in gestation gradually acquires spatial prominence at the expense of the holokinetic system. Recent work in applied psychology on the acquisition of manual skill has confirmed the important variations that occur in the correlation of the two systems with intelligence.

Haster (1948) reminds us that of the 2,200 sq. cm. of cortical surface, representing a square of 47 cm., only one-third is accessible to localizing exploration. Two-thirds are hidden, and if one considers the individual variability of convolutional form, it is obvious that the difficulties encountered in any attempt at precise localization are very great indeed.

THE FRONTAL LOBES.

The operations of prefrontal leucotomy and neurotomy, which form the subject of a separate article, have stimulated research on the functions of the frontal lobe, though here again, from the point of view of physiological psychology, additions to our knowledge other than those engendered by psycho-surgical procedures are largely based on anatomical observations. The 28th volume of the *Research Publications of the Association for the Study of Nervous and Mental Diseases* (1948) is wholly devoted to the activity of the frontal lobes. Halstead (1948) has contributed a valuable paper on specialization of biological function in relation to the frontal lobes. Two hundred and thirty-seven subjects, including 30 normal controls, were examined by a battery of 27 psychological tests. The subjects included 50 cerebral lobectomies, 63 general surgical cases suffering from war cerebral injuries, 37 neuropsychiatric patients with similar war cortical injuries, 28 civilian patients with closed head injuries, and 3 pre- and post-frontal lobotomies with subcortical lesions. Factor analyses of those variables amenable to Pearson's correlation technique and to Thurstone's multiple factor solution yielded a four-factor description of performance. These factors were found to be valid for differentiating the effects of brain injury; they have been made the basis for a four-factor theory of biological intelligence, and may be summarized as:

1. A central integrator field factor, C. This factor represents the organized experience. It is the ground function of the "familiar" in terms of which the psychologically "new" is tested and incorporated.

2. A factor of abstraction, A. This grouping factor involves the comprehension of essential similarities and differences.
3. A power factor, P. This factor operates to counterbalance or regulate the affective forces.
4. A directional factor, D. This constitutes the medium through which the other factors are exteriorized at any moment.

From these four factors Halstead derives the concept of biological intelligence expressing the total reaction of a healthy nervous system to the calls of the environment. Its lability and adaptability is by no means adequately expressed by the I.Q. Although this factorial analysis and resynthesis would appear to be too flimsy a structure to support such a massive concept, studies on these lines reveal the fact that some of the factors essential for self-consciousness have their maximal representation in the anterior portion of the frontal lobes. Halstead claims that removal of their structure reduced personality so that the capacity for growth of the ego and differentiation are lost. The mutilated personality manages to survive in terms of a highly stereotyped mode of living.

Bard and Mountcastle (1948) have studied the forebrain mechanism involved in the expression of rage, with special reference to the suppression of angry behaviour. They found that a state of extreme refractoriness to rage-producing stimuli, a condition that they term placidity, is produced in cats by bilateral removal of the neocortex without significant injury to other parts of the forebrain. It was found necessary to spare on one or both sides certain rhinencephalic structures, and at least part of the cingular gyrus and its extension above and round the rostrum of the corpus callosum. In the placid cats the amygdala, the hippocampus and the cortical fields of the pyriform lobe were left intact. The afferent thalamic projections to the retrosphenoid and cingular areas from the anterior group of nuclei were largely interrupted. A high proportion of the fibres from the anteromedial nucleus to the anterior limbic area remained intact.

Cats deprived not only of the neocortex, but also of the greater part of the telencephalon, tend to show anger on the slightest provocation. This suggests that in such placid animals if one or more parts of the forebrain remain intact they exert a continuous suppressive influence on the brain-stem mechanisms concerned with the expression of anger. The placid state could be converted to one of ferocity by either removal of the transitional midline frontal cortex or ablation of the pyriform lobe, amygdala and hippocampus. How these results are to be interpreted in terms of human physiological psychology is not so clear—even in monkeys they are irreconcilable with the directly opposite results of Bucy and Klüver, and Bard and Mountcastle admit their inability to explain this. Stimulation of the orbital surface of man prior to leucotomy by Livingstone *et al.* (1948) results in blood pressure and respiratory effects that may be cited as at any rate consistent with the occasionally recorded instances of aggressiveness and irritability with orbital lesions. Ward (1949) writes on cortical area 24 or LA of Economo in relation to personality. This area has a very powerful suppressor function. Lesions affecting this area are probably responsible for such mental symptoms as are noted in the corpus

callosum syndrome. Over and above its suppressive function, this area controls such autonomous functions as the respiratory, cardiovascular, erection of hair and pupillary dilation.

In the discussion of this paper Ward defines the suppressor area for each sector of the cortex, 8.S controlling the associative activity of the frontal lobe, 4.S controlling the motor system, 2.S somaesthesia and 19.S controlling visual function. Suppressive area 24 controls the whole motor system, together with the autonomic system.

Walker and Johnson (1948) deal with the normal and pathological types of after-discharge following the cessation of electric stimulation of the frontal cortex in the monkey. The direct relation of this phenomenon to events of psychological interest is of course obscure, though it may throw light on some types of perseverative activity in mental defectives. Robb (1948) deals with the effect of excision and stimulation of the frontal lobe on speech. This important chapter includes (1) a brief historical review of some of the background leading up to the present views on aphasia and the cerebral localization of speech. (2) Some of the experimental and clinical research on the function of the cortex is reviewed. (3) An account of 27 patients in whom cortical excisions were carried out in the left frontal lobe. In 26 of these cases there was no residual speech defect; in 16 the left hemisphere was proved to be the dominant one by the occurrence of a transient post-operative aphasia. (4) It would appear that all the lateral aspect of the left frontal lobe, with the exception of the posterior part of the third left frontal convolution, may be removed, and recovery will be possible. (5) The method of electric stimulation was used for determining the cortical areas functioning as speech centres. At the outset of the investigation it was hoped to find a method of temporarily paralysing the function of a small area of cortex for localization of speech. Injection of anaesthetic into such small areas proved to be inadequate. In the same way as electrical stimulation is used to produce movement and sensation, cortical speech function was blocked by Penfield. The patient would be asked to count, and during counting stimulation was carried out by a Rahm stimulator, set at various intensities from 3 to 4 volts. In the left hemisphere, anterior to the cerebral fissure, all the "arrest" responses but two consisted either of complete arrest of speech or slowing. The few controls done on the right Broca's area failed to produce an arrest response. On the right non-dominant hemisphere all arrest responses were linked to the sensorimotor strip controlling the muscles of vocalization. It will be noted that excisions of this type still leave the question unanswered as to whether the aphasia is due to cortical or subcortical damage.

Penfield and Rasmussen (1949) stimulated the precentral gyrus in man during cerebral operation, and succeeded in eliciting a sound like that of a prolonged vowel phonation so long as the electrical stimulation was continued. During the vocalization the patient had the sensation of an urge to call out, without attaching any precise idea or emotion thereto. If the same area which caused vocalization in the silent patient were stimulated whilst he was speaking, speech could be rendered difficult or even silenced. These effects could be obtained from both halves of the brain, but it was only in the dominant half

that stimulation of the Broca area was successful. Stimulation of Broca's area seemed to have the power of interrupting ideation. In this connection the authors do not appear to have attempted any assessment of the type of imagery usually employed. Stimulation in the dominant hemisphere of a zone anterior to the Sylvian fissure, and posterior to the precentral gyrus, either arrested speech or rendered choice of words difficult.

It would appear that not only is the anterior central convolution of importance for articulation, but that frontal and parietal areas exist which are necessary for the mental processes involved in speaking.

A symposium on thalamo-cortical relationships was held at the annual meeting of the American Electro-encephalographic Society, in June, 1949. The papers and discussions are to be found in No. 4 of the first volume of *Electro-encephalography*. From the point of view of physiological psychology, most of these very important additions to our knowledge are as yet chiefly of interest to the anatomist and the electrophysiologist. That a time will come when these new facts will be co-ordinated with psychological functions cannot be doubted. At present there are few, if any, clues to the functional significance of the bewildering complexity of thalamic organization. The concluding remarks by Earl Walker (1949) may be summarized: Rose and Woolsey (1949) have presented a classification of thalamic nuclei based on embryological considerations. Apart from the purely anatomical observations, Rose and Woolsey have emphasized the importance of the rhinencephalon in thalamic mechanisms. Considered for long as only an olfactory system, it has recently received more attention, and its role in the general integration of nervous mechanisms may soon be understood.

Jasper (1949) discussed the general organization of the thalamic systems acting upon the cerebral cortex. To the better-known relay and elaborative systems which subserve the sensory modalities he has added a thalamic reticular system which appears to act as a governor of the entire cerebral cortex.

DIENCEPHALON.

The relation of the diencephalon to cortical activity has received renewed attention during the period under review. Most of the recent additions to our knowledge depend upon the use of the electro-encephalographic method, and are dealt with elsewhere. Delay (1947), using the term consciousness as synonymous with vigilance, endeavours to show that vigilance is functionally dependent on the diencephalon, and from a review of clinical and experimental evidence, concludes that the vigilance-maintaining function of the diencephalon is exerted on and by the cerebral cortex.

Ward (1949) and McCullough (1947) have studied the projection of the frontal lobe on the hypothalamus by the method of physiological neuronography. Discrete projections have been demonstrated between areas of the cortex and the mammillary nuclei.

Murphy and Gellhorn (1946), by similar methods, traced the wide connection between the hypothalamus, the ventrolateral and dorsomedial thalamus, and the cortex in the cat.

The suppression of cortical activity in its bearing on the problem of sleep by diencephalon stimulation is of great interest to psychiatrists, in view of the suggestive evidence pointing to a diencephalic origin of schizophrenic psychoses. Gualtierotti, Martini and Marzorati (1949) claim to have produced inhibition of cortical activity by stimulation of the diencephalon with square waves at a frequency of 280 cycles per second.

Ranstrom (1947) points out the difficulty of reconciling the opposed views of Hess and Ransom on sleep-regulating function of the hypothalamus. Whilst Hess was able to induce sleep in non-anaesthetized cats by electric stimulation of the posterior part of the hypothalamus with weak currents, Ransom and his pupils produced sleep by causing lesions of this part of the brain. Ranstrom attempts to reconcile these contradictory views. He believes that stimulation of the hypothalamus causes the liberation of a sleep-promoting substance acting on other parts of the brain. Whereas with stimulation only a small amount of this substance is liberated, a destructive lesion may cause liberation of larger amounts of this hypothetical substance. These views are supported by experiments on cats, and it is claimed that after a lesion of the hypothalamus has been effected sleep does not start immediately, but some hours later. An attempt is made to substantiate these views by some biological evidence of the existence of neurosecretion in the hypothalamus.

Consciousness and its disturbances, is the subject of two papers by Martin (1949). These are summarized by the author in the following terms: Consciousness depends on the activity of the cerebral cortex. There is no evidence of conscious activity in man resulting from the activity of other structures in the absence of cortical activity. Impairment of cortical activity over a wide area leads to unconsciousness. The activity of the cortex with which consciousness is associated is maintained in some vegetative way by activity of the hypothalamus. Unconsciousness may therefore be caused by lesions of the hypothalamus. The activity of the cortex with which consciousness is associated is maintained by afferent impulses in the sensory systems. Unconsciousness may be caused by interruption of the somatic sensory tracts in the upper half of the brain stem; this is probably because all awareness of the body is thereby abolished, and some awareness of the body is necessary for consciousness. Consciousness is usually associated with the presence of fast rhythms in the electro-encephalogram, and sleep and coma with the absence of such rhythms, but fast rhythms may be present during unconsciousness. Sectional disturbances of consciousness are due to the impairment or loss of some afferent activity which abolishes the awareness of part of the bodily self or its environment. Dreamy states and psychical seizures are sectional disturbances, and may be likened to a double partial consciousness (one true and one false). Much of our activity is outside consciousness, but some record of willed movement may be made in consciousness.

Closely allied to the problem of sleep is that of hypnosis. Recent investigations from the physiological point of view have thrown little light on this condition. Gorton (1949) has failed to find evidence of any physiological difference between the waking and the hypnotic state. Although the suggestibility differs so markedly from that obtainable in the normal state, nothing

seems to be known of the basic mechanisms involved as distinguished from the psychical factors.

CONDITIONED REFLEXES AND EMOTION.

The work in the period under review on conditioned reflexes exhibited by individual organs of the general somatic system promises to furnish a physiology of the affective states or emotions.

Such a physiology has been long overdue. Although the writer, using the so-called psychogalvanic reaction, was able in 1921 to demonstrate the formation of a conditioned reflex in man which involved one of the bodily concomitants of an emotional event, this has not yet led to the study of the physiology of the various bodily responses in detail, and an attempt to determine how they, in combination, give rise to the sensory complex of the affective state. It is in this context that the work of Bykof assumes great importance, in that it has thrown new light on the manner in which the various organs—the respiratory system, the vascular system, the gastro-intestinal tracts, the kidneys, liver and spleen—can furnish conditioned reflex responses. Thus in dogs with externalized ureteral orifices diuresis could be established as a conditioned reflex, the filling of the rectum with water being the unconditioned stimulus. Secondary and trace conditioned reflexes could also be produced.

It was also found possible to evoke inhibitory conditioned reflexes of the specific organs. Thus, the action of pituitrin as an inhibitor of urinary secretion could be employed in establishing an inhibitory conditioned reflex. The kidney conditioned reflex can, according to Bykof, be equally well evoked either by nerve, or in the case of the denervated organ, by humoral agency.

A similar double agency was demonstrated for conditioned reflex activity in the shape of splenic contractions. Thyroxine being used as an unconditioned stimulus affecting basal metabolism, a conditioned reflex was elicited to a signal. In thyroidectomized animals no conditioned reflex to basal metabolism could be found. The work of Bykof is at present inaccessible to those who are unable to read Russian, and the foregoing account of his work is to be found in the article by Gantt (1948) in the *Annual Review of Physiology*.

Gantt (1947) and his co-workers have made important observations on the cardiac conditioned reflexes. They claim to have demonstrated a specific cardiac conditioned reflex on the basis of both excitation and inhibition to food and painful stimuli. Using the cardiac conditioned reflex, Robinson (1947) and Gantt were able to establish a conditioning of sexual excitation through the cardiac component, and a similar attempt seems to have been obtained with the inclusion of the cardiac component in the orientating reflex. A cardiac time reflex was established by Gantt as a conditioned reflex.

That the affective state known as emotion occurs as a conditioned rather than an unconditioned response in human sensory experience is sufficiently obvious, but so far the somatic affective complex has eluded analysis. These studies of visceral conditioned reflexes may encourage workers in the field of physiological psychology to attempt some form of differential classification of emotional states, the implications of which, in the study of the psychopathology of affective states, are obvious.

The direct studying of emotional states by physiological methods has, during the period under review, yielded on the whole no very novel results. Attempts such as those of Diethelm, Doty and Milhorat (1945) to demonstrate autonomic and cholinergic changes in the blood, in emotional conditions, by the effect on the duodenum of the rabbit, though interesting, can hardly succeed without much greater attention to the obvious sources of fallacy that will suggest themselves to anyone familiar with physiological techniques. The earlier work of Cannon (1929, 1935), on the effect of emotion on gastric secretion and vasomotor reaction, has received additional confirmation from the observations of Szasz (1948) in a case where anger stimulated the production of a large volume of HCl, and this was abolished by double vagus section.

An account of recent work of Wolf and Wolff (1944) has been given in a very valuable summary of our present knowledge of the physiology of the emotions by Samson Wright (1949). The original work of Wolf, although two years anterior to the period under review, escaped notice in the preceding volume of this series. The observations were carried out on a man with a chronic gastric fistula. The vascularity of the gastric mucosa, the secretions and the motility of the stomach were recorded. Sudden fear, owing to the dramatic entrance of the physician, caused intense vasoconstriction of the gastric mucosa and a marked diminution of gastric secretion and the percentage of HCl. A condition of depression with sadness and self-reproach led to a decreased response to the ingestion of broth. Broth ingestion in a normal state led, of course, to a marked increase of vascularity and of gastric secretion and acidity, but whilst the patient was in his depressed and sad condition the broth caused no appreciable increase in vascularity, and only a very slight increase in acidity and gastric secretion. When a state of hostility and resentment had been aroused by unjust and rude rebukes there was an instant and marked increase in gastric vascularity, an increase in acid secretion and, accompanying these changes, an increase in gastric motility. It is of course possible that the increase in acidity might in the circumstances have been linked with a feeling of anxiety rather than hostility. In the observations of Hoezl (1942) a state of anxiety following on a gangster incident led to an increase in acid secretion lasting ten days till the incident was closed. It may be noted that in the Wolff observation the state of sudden acute fear had the opposite effect.

An attempt to demonstrate the effect of chronic fear on the gastric secretion of "muted" dogs is recorded by Mahl (1949). The seven dogs were kept in cages with an electric grid and, by means of a commutator, were subjected to a powerful shock accompanied by a buzzer at irregular intervals every few minutes, night and day, each animal receiving 75 stimuli every 12 hours, and this inhuman experiment continued for a whole year on the same animals. As might have been expected, the behaviour of the animals was far too abnormal to warrant any conclusions from the gastric analysis; they lay for the most part motionless, crouched on the floor of the cage, and had to be stirred with a stick. The general disapprobation which these experiments received (*Lancet*, 1949) should make the employment of such methods impossible in the future. Verney (1946) has furnished evidence that the posterior pituitary secretion

of antidiuretic hormone is increased in certain emotional states, since the concomitant diuresis from ingestion of large amounts of water is inhibited. It may be noted, in conclusion, that until we know something of the effect arising from the change of state or function of each organ involved in the conditioned emotional reaction, and their combined effect on the sensorium, we are hardly likely to make much progress in the study of the physiological psychology of the emotions. There is at present no knowledge of the origin of the sensory experiences that combine to form the emotional state.

Unwelcome though it may be to those of us who have deeply-rooted prejudices as to the relation of changes in tissue organization and function to mental events, there is a body of evidence that can no longer be ignored, pointing to the occurrence of specific physiological and anatomical tissue reactions illustrating mental processes and persisting after the cessation of the mental event, corroborating the older evidence.

Noel Harris (1949) records a number of instances of stigmata occurring during abreaction, and appends a photograph of a physical condition which reproduced a trauma that had been incurred some years previously under emotional and dramatic conditions. Similar photographs, both of the skin and the blood-stained dressing, made by R. L. Moody are also given. The accounts, like many in the past, seem to exclude trickery on the part of the patient. Viewed in the light of some of the work of Bykof and Gantt previously alluded to on the visceral conditioned reflexes, the difficulties that the physiologist must feel about their acceptance are at any rate appreciably alleviated.

ENDOCRINOLOGY.

An important survey of interrelationships between endocrine secretions and patterns of overt response has been made by Professor Beach (1948), and the book should be in the possession of everyone interested in this aspect of physiological psychology. Owing presumably to delay in publication, none of the literature quoted is of more recent date than 1945, and hence does not come within the scope of the present survey. The additions made by endocrinological research to physiological psychology since the survey of Beach have, however, been disappointingly few, although endocrinology, in the service of psychiatry, has contributed much that should undoubtedly serve as a pointer to many purely psychological considerations.

Sexual hormones.—The effects of castration on male sexual behaviour have recently received much attention. This subject is of some medico-legal importance, in view of the incessant demand for surgical treatment of criminals convicted of repeated sexual misdemeanours. Golla and Hodge (1949) have collected both recent and older data on the effect of castration on libido in adult men, and there can be no doubt that libido is by no means always abolished by removal of the testicles. The conclusion seems to be inescapable, that an image of the whole complex of libidinous activity may persist in certain circumstances, just as the image of the phantom limb with imaged movement may occur after amputation at the hip or knee-joint.

It is a further point of interest that, though libido in the male may be eliminated by the effect of intensive treatment with female sex hormones

on pituitary activity, as exemplified in the treatment of acromegaly, it returns on suspending the oestrone administrations; but even when the oestrone treatment is causing inhibition of libido, adding testosterone propionate to the oestrone injections will restore libido. Inasmuch as castration does not necessarily abolish male libido, it seems probable that it is not the indirect action of oestrone on the testicles that is responsible for its inhibition, but rather an effect mediated by the pituitary on the nervous mechanisms concerned.

Clark and Back investigated the effect of sex hormone on the sexual status of male castrate chimpanzees. They found evidence that after testosterone injections the male castrates show definite resumption of dominance over the female.

The same authors (1946) found that the social dominance status of the female castrate chimpanzee is definitely enhanced on raising the oestrogen level. Administration of androgen had a similar effect in raising the social status of the female castrate, though in that case the secondary tumescence of the pudenda was of course absent.

Psychological evidence of the effect of testosterone propionate on nervous mechanisms, other than sexual, is adduced by the observation that the flicker fusion threshold is raised. This effect does not appear to be sex-linked.

Corticotrophic hormone is stated to have some stimulating effect on general mental activity.

On the whole, the rapid advance of the past five years in endocrinological knowledge, though it has given some further insight into the pathology of endocrinological disturbances associated with mental disorders, cannot be said to have as yet led to any specific psychological information.

PAIN.

Consideration of the physiological psychology of the special senses, although logically admissible, cannot be treated within the limits of this review. The attention given in the review period to certain aspects of the physiological psychology of pain may, however, be briefly summarized. Wikler, Goodell and Wolff (in Wolff, 1945), by their analysis of the action of analgesic drugs, have brought additional proof to that afforded by chordotomy as to pain being a specific sensory expression served by its specific neural mechanisms. Thus they show that morphine, amongst other drugs, can be given in such dosage as to raise the threshold of pain sensation up to 80 per cent. above the normal level without affecting the threshold for touch, hearing, smell or warmth, or without impairing compass-point discrimination or the perception of vibration. Such results could also be obtained with appropriate ethanol dosage.

Wolff (1948) and his associates produce new evidence, quoted in Wolff's monograph on headache, of the absence of spatial summation for pain, and point out that the intensity of pain depends on the intensity of the stimulus, and not on the size of the area involved, although, of course, the mental distress will be dependent on the apperception of both factors. Bigelow (1945) and his co-workers claim to demonstrate two types of pain sensation, one type

of pain being abrupt in onset and leaving a pricking quality that quickly terminates; the other type, slow in onset, never reaches an abrupt or pricking climax and recedes more slowly. Using the radiation pain-producing technique of Hardy and Wolff they showed that both types of pain have the same absence of spatial summation, and their threshold is in both cases raised by alcohol.

Wolff (1948) demonstrated that in some conditions the burning pain threshold may be lowered without affecting that of the pricking type.

Theobald (1949), in a study of the role of the cerebral cortex in the apprehension of pain, comes to the following conclusions: He considers that the phenomenon of referred pain cannot be explained, either on the assumption that a "commotion" in the spinal cord could affect other afferent nerves entering the same segment of the cord, or by postulating changes, whether caused by the liberation of metabolites or angiospasm in the cutaneous areas of reference. In addition, the localization of visceral and proprioceptive pain could not be thus explained.

He postulates that impulses travelling along afferent nerves that mediate the sensation of pain, whether from the skin, the deeper structures of the body, or the viscera, ultimately reach the same area of the cortex as do the tactile and thermal impulses, and that this makes localization possible.

SMELL.

Adrian (1948) has summarized our knowledge of the sense of smell in a comprehensive review dealing especially with the electrical responses obtained from the olfactory lobes to stimulation of the nasal mucosa. The methods employed are of necessity physiological, but point to certain conclusions of psychological importance, amongst others that it is highly improbable that the human being possesses specific receptors for all the odours he is capable of recognizing, but more probably that the odour is produced by mixtures of excitations of a limited number of neuronc terminations of different types.

APPETITION.

The earlier observations of Richter and others on appétition—a process of self-regulating activity depending on the sense of taste, and tending to maintain the state of internal equilibrium necessary for efficient vital functioning—was of course founded on animal experiments. The work of Mayer-Gross and Walker (1948) on the taste and selection of food in hypoglycaemia has allowed the extension of such observations to man. The subject thus demands consideration in any account of physiological psychology. Their paper is based on 202 experiments carried out in 100 subjects, with the object of testing self-regulation in different stages of hypoglycaemia. The subject was offered a choice of five liquids—water, 5 per cent. sucrose, 30 per cent. sucrose, 0.5 per cent. sodium chloride, and saccharine. His preference, judgment of taste and other reactions were noted when the blood sugar was reduced by causing various degrees of hypoglycaemia by insulin administration. Preference was given to 30 per cent. sucrose solution when the blood-sugar

level fell below 50 mgm. per cent. When it was above this level the 30 per cent sucrose solution was rejected. Saccharin solution of equal sweetness with the 30 per cent. sucrose was rejected in favour of the sucrose when the blood sugar sank below 50 mgm. per cent.

A depression of the power of recognizing sweetness occurs when the blood glucose falls below the 50 mgm. per cent. level, but salt and bitter tastes are undisturbed. There appeared to be a specific depression of the tongue receptors dealing with sweet taste which reversed the normal dislike of the excessive sweetness of 30 per cent. sucrose to a preference. The apparent refinement of discriminatory power that allows the subject to distinguish the sucrose solution from saccharin of equal sweetness still requires some explanation.

PHARMACOLOGY.

The action of alcohol continues to provide urgent problems for solution in physiological psychology. The recent Scandinavian work has shown that administration of tetraethyluram sulphide will potentiate the toxicity of ethanol to such an extent that a very small amount of alcohol may cause serious and disturbing symptoms. This work promises, quite apart from its importance as a means of conditioning alcoholic addicts against the drug, a clue as to the way in which alcohol affects the nervous system. At first sight the formation of very large amounts of acetaldehyde, when ethanol is ingested in the presence of the tetraethyluram, might suggest that alcoholic intoxication is really due to acetaldehyde, which is of course also formed in considerable quantity after ingestion of alcohol alone. The amount of acetaldehyde present in the blood even with severe alcohol intoxication in the absence of the tetraethyluram does not, however, support this hypothesis.

From the psychological angle, by far the most interesting new facts presented by Masserman (1948) are the effects of alcohol on experimental neurosis in cats. A cat was made neurotic by the breaking up of trained adaptive behaviour with a frustrating noxious stimulus. A normal cat prefers plain milk to milk with a low percentage of alcohol. If, however, a neurotic cat is induced to partake of the milk-alcohol mixture, not only do the neurotic symptoms tend to disappear, but the cat for a time will show a preference for the alcohol mixture which ceases with complete recovery from the neurotic condition.

In the Kelyack lecture of the Society for the Study of Addiction (Golla, 1949) a more probable explanation of the appetite of the neurotic cat for alcohol was attempted than that advanced by Masserman. Masserman thinks that the cat recognized the steadying effect of alcohol on its disordered nerves, which argues a rather improbable power of self-analysis. Just as in the experiments of Mayer-Gross, detailed above, the appetite for glucose is conditioned by the sugar content of the blood, it is not unthinkable that a disturbance of nervous metabolism may produce an appetite, not, of course, for alcohol *per se*, but for substances possessing the property of alcohol to affect a neurotically conditioned disturbance of the carbohydrate metabolism of the brain. It was pointed out that similar appetitions have been produced in the experiments of Richter and others on rats with various artificially produced deficiencies.

GLUTAMIC ACID.

Ever since the initial observation of Price and Putnam as to the alleged power of glutamic acid to control minor fits in idiopathic epilepsy, and the increase in mental alertness shown by cases so treated, there have been a series of conflicting observations on the mind-stimulating power of glutamic acid. It is difficult to avoid the suspicion that the mongols and other deficient children said to have benefited might have been influenced in their mental development by the attention that they received. Some of the later work of Zimmerman, Putnam and Burmeister (1947) seems to have definitely shown that the alleged effects on mental development do not occur in normal adolescents, and Marx (1948) similarly fails to confirm the effect on maze learning in rats.

Richter Dawson, and Rees (1948) found that the glutamin content of the rat's brain was not significantly affected by physical or emotional stimulation.

Levene *et al.* (1948) have assayed the physiological and psychological effects of intravenous injection of pervitin 20 mgm. in comparison with 250 mgm. sodium amytal and 20 mgm. amphetamine. Amytal had the greatest effect in psychic tension. Pervitin was more powerfully cephalotropic and sympatheticotrophic than benzedrine.

Goetzl and Stone (1948) determined the influence of amphetamine on olfactory acuity and appetite. It was found that amphetamine sulphate (10 mgm.) is capable of simultaneously producing a decrease in olfactory acuity, a decrease in intensity of the sensation of appetite, a decrease in freely selected caloric intake, and also of producing a feeling of satiety.

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NEURO-ENDOCRINE RELATIONSHIP AND ENDOCRINOLOGY IN CLINICAL PSYCHIATRY.

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In the previous edition of *Recent Progress in Psychiatry* the authors contributed chapters on neuro-endocrine relationships and on endocrinology separately. These have now been combined under the above heading, since relatively little that is fresh has been published in the field of endocrine treatment in psychiatry, but important developments in investigation methods have widened the scope of research, and broadened or modified views previously expressed.

NEURO-ENDOCRINE RELATIONS.

There has been no further work pointing to a direct influence of the nervous system on the peripheral epithelial ductless glands. Neural stimulation and inhibition are transmitted and mediated by the pituitary anterior lobe. Peripheral glands, especially the thyroid, which appear to be under the direct influence of the autonomic nervous system, are now believed to be controlled, not by direct innervation of the secretory cells, but by modifications of the blood supply.

An exhaustive review of neural control of the pituitary gland has been published by Harris (1948), from which it would appear that the previous conceptions of the neural control of the pituitary anterior lobe require to be revised.

Harris points to the conflicting evidence about interference with adeno-hypophyseal function that follows pituitary stalk section, and to the scarcity of nerve fibres in the pars distalis, and says that the evidence that pituitary activity is under the influence of the peripheral autonomic nervous system is not convincing. The pars distalis is described as a gland under nervous control, but lacking a nerve supply.

There is, according to Harris, much experimental and clinical evidence that the hypothalamus is functionally linked with anterior pituitary activity. The most direct route by which this influence might be exerted is through nerve fibres or blood vessels of the hypophyseal stalk—almost certainly not the former. However, the portal vessels of the stalk, unlike the nerve fibres, may undergo repair following stalk section and so re-establish humoral transmission of the stimuli to the pars distalis.

Harris describes "small arterial twigs running from the internal carotid and posterior communicating arteries to supply a large vascular plexus situated between the pars tuberalis and the median eminence. From this plexus very characteristic sinusoidal capillary loops penetrate the median eminence, where

they are surrounded by the wealth of nerve fibres of the hypothalamico-hypophyseal tract. These capillaries then pass into large trunks which run down the hypophyseal stalk, draining into the pars distalis where the blood is redistributed by the large sinusoids of the gland. The pattern differs in detail in different animals; in the human the upper system of capillary loops and tufts being present in the infundibular stem as well as the median eminence. Nerve fibres of the hypothalamico-hypophyseal tract, besides being intimately related to the sinusoidal loops in the median eminence, pass in moderate numbers into the pars tuberalis, where they may be seen associated with the vascular plexus."

The assumption of Harris is that neural control of the adeno-hypophysis is humerally transmitted from the neuro-hypophysis to the pars distalis. According to him, nervous stimuli might possibly liberate such substances into the capillary sinusoids of the median eminence, these substances then being transported via the hypophyseal portal vessels to excite or inhibit the pars distalis. Differences in results after experimental section of the pituitary stalk are explained by Harris by variations in the degree of regeneration of the hypophyseal portal vessels. In support of this he cites experiments where, after transection of the stalk, small metallic plates were put between the divided ends, and gonadal atrophy followed, and where injection by indian ink of the vascular tree of rats, after division of the stalk, indicated regeneration of the hypophyseal portal vessels.

So far, leucotomy has not fulfilled the hope that it would throw fresh light on the physiological relationships between brain and endocrine function. Indeed, after leucotomy quite inconstant and variable alterations in thyroid and adrenal cortex activity have been observed; increase, no change, and decrease of both have been reported.

We have noticed that mental improvement is frequently associated with increase in thyroid and adrenal cortex function (tracer investigation, and 17-ketosteroid and cortin excretion) after leucotomy. However, constant endocrine results are not to be expected, having regard to the great differences in the anatomical localization of the surgical lesions, quite apart from unknown factors introduced by the mental illness itself. (See also McLardy and Meyer, 1949).

NEURO-ENDOCRINE ANALYSIS IN MENTAL DISEASE.

So many contributions have been made in recent years to show functional disturbances of different ductless glands in various psychiatric conditions, that it is somewhat confusing to enumerate and discuss the psychiatric entities and associated endocrine disturbances reported by different authors.

It is important to ascertain how far endocrine disturbances are primary causes or secondary consequences of psychopathological conditions, and how far coincidental disturbances exist independently.

As one-quarter to one-third of the total metabolism of the body takes place in the brain, extreme metabolic disorders (as, for example, hunger) can produce quite different psychological pictures, apparently depending upon the reaction type of the brain or of mental constitution.

Disturbances of various ductless glands do not of necessity produce the same kind of reaction in different individuals. Thyroid abnormality, for example, may produce no marked mental alteration in some, and in others slowing or acceleration of mental processes or even a psychotic episode.

These facts, however, do not mean that the reaction type of the brain to other disturbances of environmental metabolic and endocrine nature cannot be influenced by different hormones.

An exhaustive survey of inter-relationships between endocrine secretions and patterns of overt response has been published by Beach (1948).

A number of papers purport to show changes in the electroencephalogram in various endocrine disorders. No doubt the changes described are not specific for the disorders, but reflect the influence of various hormones, or their lack, on the neuro-physiological networks. Relevant papers are as follows:

Lindsley and Rubenstein (1937), Bertrand, Delay and Guillaín (1938), Hoagland (1938), Ross and Schwab (1939), Bertrand, Delay and Guillaín (1939), Gibbs and Gibbs (1941), Himwich, Daly, Fazekas and Herrlich (1942) dealt with E.E.G. and thyroid disturbances.

Odoriz *et al.* (1943) studied the E.E.G. in parathyroid insufficiency.

Fournier and Torrents (1942), Hoffman, Lewis and Thorn (1942), Engel and Margolin (1942) studied the E.E.G. in adrenocortical underfunction and in Addison's disease.

Engel and Romano (1944), Gellhorn and Ballin (1946), McQuarrie (1946), Grenell and McCawley (1947), Aird *et al.* (1947), Grenell (1947), Grenell and McCawley (1947) studied also the influence of desoxycorticosterone and of cortin extracts on the E.E.G.

De Barenne and Gibbs (1942) studied E.E.G. during the menstrual cycle; Gibbs and Reid (1944) during pregnancy; and Cress and Greenblatt investigated the influence of stilboestrol and progesterone on the E.E.G.

Hoagland, Rubin and Cameron (1937) studied the E.E.G. on schizophrenics before and after treatment. More recent investigations of the E.E.G. in connection with insulin treatment and sugar combustion of the brain were published by Knott and Gottlieb (1943), Gellhorn and Kessler (1943), Greenblatt, Murray and Root (1946), Baisset *et al.* (1947).

Wikler (1947) investigated the effects of pitressin hydration on the E.E.G. See also Blier and Redlich (1949), Cohn, Kolb and Mulder (1947).

Hoagland *et al.* (1946) reported on changes in E.E.G. in correlation with changes of 17-ketosteroids in states of agitated depression.

THYROID.

Interest in the relationship between thyroid and mental illnesses has once more increased in recent years. The conclusion of Danziger and Kindwell (1948), that deficient oxidation in the brain is a potent factor in the causation of some mental disorders, now seems probable. These authors treated 5 psychoneurotic patients and 19 psychotic patients (manic-depressive and schizophrenic) with very high doses of dried thyroid extracts or thyroxin, and

claim recovery in all the psychotic and two of the psychoneurotic patients. They suggest that similar results might be obtained by the additional use of other oxidation promoters.

Delay *et al.* (1948) deny that any causative relationship between thyroid disorders and manic-depressive psychosis has been established, in spite of the difficulty of differentiating between certain cases of manic-depressive psychosis and Graves' disease. Zondek and Wolfsohn (1944) report a patient who developed a schizophrenic reaction after childbirth. When, 18 months later, hypothyroidism was found and treated with thyroid, the patient recovered within 2 weeks and remained normal a year later.

Medvei (1949) has described psychotic reactions which developed several months after subtotal thyroidectomy, with complete disappearance of symptoms after thyroid treatment for a week.

Asher (1949) published a series of cases in which he claimed that thyroid under-function had been accidentally discovered, and in which thyroid treatment produced significant improvement. His series included no specific types of mental disorder. The majority of his cases were seriously ill—in much reduced mental and physical health.

According to Means (1948), mental reactions, even amounting to a psychosis, in thyrotoxicosis, are determined by the mental make-up of the patient, the thyrotoxicosis activating latent trends. Occasionally the mental abnormality vanishes, after treatment with iodine alone, but in certain cases correction of the thyroid disorder is not followed by a corresponding mental improvement.

Until the introduction of radio-active tracer methods (referred to later), the diagnostic methods were too unreliable to allow for systematic investigation of the relationship between thyroid function and psychopathological conditions.

In spite of encouraging results claimed by Hoskins and others, therapeutic benefit from thyroid in psychiatry, in the hands of most workers, has been so disappointing that this treatment has fallen into some discredit. This appears due to the lack of clear-cut indications and the inaccuracy of the available investigation methods. Radio-active tracer technique with I^{131} should do much to alter the situation.

Hemphill and Reiss (1950) have elaborated the tracer method so that thyroid function can be accurately measured within very fine limits, even in borderline cases. An initial survey of 400 patients of a mental hospital showed: (1) that female patients tend to have a higher level of thyroid function than males, and (2) that definite hypothyroidism occurred in 50 per cent. of male cases with clinical anxiety, as compared with nearly 50 per cent. normal and 50 per cent. hyperactivity in females.

Thyroid underfunction in male anxiety was tentatively explained as a consequence of disturbed circulation rate in the thyroid, the result of chronic hyperadrenalinaemia, which prevented the thyroid from taking up sufficient iodine. This was demonstrated in animal experiments, when rabbits were injected simultaneously with adrenalin and I^{131} ; the iodine uptake was then significantly reduced.

Reiss *et al.* (1949), using radio-active technique, showed that in chronic psychotic patients there existed primary and secondary hypothyroidism.

In the former, treatment with thyrotrophic hormone failed to produce increased thyroid activity, while in the latter there was an increased uptake of I^{131} . In the second class of patients there is obviously a primary pituitary disturbance, and the hypothyroidism is the result of inadequate thyrotrophic hormone. If small doses of I^{131} are used according to a special technique, investigations with tracer can be repeated and the response to various forms of treatment, including psychotherapy, and its influence upon the thyroid can be studied.

ADRENAL CORTEX.

Since the publication of the previous edition of *Recent Progress in Psychiatry*, the adrenal cortex has assumed great importance in general medicine and psychiatry. Hemphill and Reiss (1942) emphasized the close correlation between the pituitary, adrenal cortex system, and certain mental disturbances. They described a form of involutional melancholia where treatment with a purified biologically-standardized corticotrophic hormone brought about improvement in appetite and general physical condition, loss of depression and delusions of visceral illness, and with these a rise of the 17-ketosteroid excretion. For comparison—the dose of corticotrophic hormone they administered equalled $1-2\frac{1}{2}$ mgm. of the adrenocorticotrophic preparation used at present (Reiss, 1949). They expressed the opinion, in connection with these and other investigations reported in the previous edition, that the therapeutic mechanism of procedures like electro-shock treatment and leucotomy are closely connected with this pituitary-adrenal cortex-brain relationship, more corticotrophic hormone being mobilized by these procedures. Numerous physiological and clinical investigations, published in the meantime, have further clarified the relationship between production of adrenocorticotrophic hormone by the pituitary anterior lobe, the release of adrenocortical hormones and their biological action, and the possible relation of these endocrine factors to brain function. For reviews of pituitary-adrenocortical relationship, see Reiss (1947), Sayers and Sayers (1948). Selye (1949) collected the different data concerned with the body reaction to stress under the general title of adaptation syndrome and alarm reaction.

Thorn and his co-workers (1948) used comparatively high doses (25–40 mgm. daily) of adrenocorticotrophic hormone in carrying out extensive investigations on the biochemical response of different patients to adrenocorticotrophic hormone. They summarized their findings after injection of A.C.T.H. in normal subjects as follows:

1. Sodium and chloride retention with increased potassium excretion. This is consistent with an increased liberation of desoxycorticosterone-like steroids.

2. An increase in fasting blood-sugar level, a significant increase in uric acid excretion accompanied by a small inconsistent rise in total nitrogen excretion, and a fall in lymphocytes and eosinophils. These changes are similar to those which have been observed following the administration of crystalline adrenal 11, 17-oxysteroids (Compounds E and F). Further indication of increased liberation of "S" hormones

is to be found in the augmented urinary excretion of 11-oxysteroid substances.

3. An increased urinary 17-ketosteroid excretion which suggested that the secretion of adrenal androgens had been stimulated.

These changes were, as Thorn (1948) pointed out, dependent upon an intact adrenal, as shown by control studies on patients with well-established Addison's disease, who failed to respond to A.C.T.H. The changes seen after A.C.T.H. were obviously not a direct action of this hormone, but rather mediated through adrenocortical steroids mobilized under its influence. Thorn *et al.* (1948) realized that the biochemical reaction to A.C.T.H. can be used as a test of adrenocortical functional capacity. They have succeeded in simplifying the test for routine use. They described a fall in eosinophils and rise in urinary uric acid/creatinine ratio four hours after injection of 25 mgm. A.C.T.H. In Addison's disease little or no significant decrease of eosinophil cells occurred after A.C.T.H. This was due to failure of the adrenal cortex to respond, since in normals injection of A.C.T.H. produced a decrease.

The test procedures were later extended in order to give some information about the ability of the pituitary anterior lobe to produce A.C.T.H. Vogt (1945) and Long (1947) had shown in animals that adrenalin was capable of stimulating the mobilization of A.C.T.H. from the pituitary anterior lobe. Thorn and his co-workers elaborated an intravenous adrenalin test where they infused 0.2 to 0.3 mgm. in 200 ml. saline over one hour, and found a considerable decrease of the eosinophil cells in normal subjects, while patients with pituitary insufficiency failed to respond. The meaning of the adrenalin test, however, is still hypothetical, since it seems possible for adrenalin to have an effect on the adrenal cortex even when the anterior lobe is removed. (Gaddum 1949; Sayers, 1949).

There are several other means of getting information about the ability of the pituitary anterior lobe to mobilize adrenocorticotrophic hormone. Pincus (1947) reported how normal men responded to the stress of exposure to cold, heat, and pursuit meter operations by increased urinary output of 17-ketosteroids and a fall of blood lymphocytes, reactions obviously due to increased endogenous mobilization of A.C.T.H. Emadjian *et al.* (1946) showed lymphocytopenia after glucose administration. The same authors reported that some psychotic men failed partially or entirely to show these responses.

Reports of very extensive investigations were published recently about the pituitary-adrenocortical function in normal and psychotic men. (Pincus *et al.*, 1949). They employed four procedures to test the pituitary-adrenocortical function in mental patients, as compared with normals: the oral glucose tolerance test (Exton-Rose), the operation of pursuit meter, the target ball frustration test, and the administration of A.C.T.H. In order to test the responsivity of the end organs affected by adrenocortical secretion, cortin was injected. Lymphocytes, amino-acids, and inorganic phosphate in blood, 17-ketosteroids and the uric acid/creatinine ratio in urine were investigated in 36 normals and 34 schizophrenics. The authors found that the patients failed to exhibit adrenocortical response to A.C.T.H. and stress, while they responded like normal subjects to adrenal cortex extract. Contrary to this,

responses were all normal in psychoneurotic patients. Many of the test results in schizophrenics published by these authors are similar to those reported by Thorn *et al.* in Addison's disease.

Altschule *et al.* (1949) have found that urinary excretion of uric acid increased after electrically-induced convulsions in man. This increase is maximal approximately four hours after electro-shock, and thereby resembles the finding in man after injection of A.C.T.H. The authors assume that electro-shock increases production of 11-oxycorticosteroids. Hoagland *et al.* (1950) claimed that electro-shock stimulates adrenal activity to a degree comparable with the injection of approximately 100 mgm. A.C.T.H. They have also suggested that favourable prognosis in electro-shock therapy in schizophrenics is commensurate with the degree of responsivity of the adrenal cortex to doses of 25 mgm. A.C.T.H. Patients with a higher degree of responsivity benefit most from insulin treatment.

There is possibly some analogy with Addison's disease. Apathy, negativism and paranoia, psychoses with paranoid features and hallucinations, and marked personality changes have been described in Addisonians. (See Engel and Margolin, 1941; Gorman and Wortis, 1947; Cleghorn and Graham, 1949; Hartman and Brownell, 1949). Hoskins claimed success in treating schizophrenics with adrenal cortex extracts. Beneficial results with desoxycorticosterone acetate on 9 schizophrenics and 6 manic-depressives were reported by Jens (1949).

That adrenal cortex function influences psychological activity has been evident and has attracted interest since the sensational results published by Hench *et al.* (1949) on rheumatic patients treated with 17-hydroxy-11-dehydrocorticosterone (Compound E). These and other investigators reported dramatic changes in the mental outlook (even euphoria) 24 hours after commencement of treatment. Similar changes are also reported after treatment with A.C.T.H. Because of the shortage of Compound E and A.C.T.H., very few investigations have so far been carried out on mental patients.

Reiss *et al.* (1950) have carried out adrenal-response tests on 70 chronic and 8 acute schizophrenics and about 50 other mental patients. Only two tests were carried out: (1) The response to 25 mgm. A.C.T.H., in order to see the reaction ability of the adrenal cortex. (2) The response to 150 gm. glucose given orally.

The response to glucose was, in the greater number of chronic schizophrenics, negative. The response to A.C.T.H., however, was, contrary to the findings of Pincus and Hoagland, positive in over 70 per cent. of all cases. There are, however, certain features seen in the response investigations which might explain some of the controversies which are bound to arise in the future. These are mainly due to the fact that the changes in eosinophils, in the uric acid/creatinine ratio and the ketosteroid excretion, seen four hours after injection of A.C.T.H., are by no means always parallel. The eosinophil counts, for instance, of chronic schizophrenics are very often decreased by over 50 per cent. four hours after injection of A.C.T.H., while the uric acid/creatinine ratio and ketosteroid excretion are unchanged or even decreased instead of increased. It occurred in some (but much fewer) patients that the uric acid/

creatinine quotient went up, while the eosinophil count was changed only insignificantly. The tentative deduction made from these discrepancies is that different hormone compounds mobilized from the adrenal cortex are responsible for changes in eosinophil count, and, for instance, ketosteroid production and excretion, or that certain functions only of the adrenal cortex are impaired and cannot be stimulated.

Hemphill *et al.* (1950) have treated a number of mental patients who gave a positive adrenal cortex response to A.C.T.H. Results of only 9 patients are available so far, some positive and some negative. Their results are, however, by no means discouraging. They only indicate that it would be futile to start therapeutic trials without establishing most rigid laboratory control. The situation existing may be compared with insulin treatment, which could not possibly be carried out successfully without controlling blood sugar. Equally necessary is the daily investigation of 17-ketosteroid and cortin excretion of patients treated with A.C.T.H. These facts will be discussed later in connection with the steroid metabolism. Here it may be pointed out first that the success of A.C.T.H. treatment will depend largely on the ability to find the right equilibrium between new production and mobilization of steroid hormones in the adrenal cortex.

GONADS.

Some further evidence about the influence of sex hormones on more general symptoms connected with brain circulation and more specific functions, like normal and pathological sex drive, has been supplied by recent papers.

Carter, Cohen and Shorr (1947) review the premenstrual tension, a term usually applied to a variety of symptoms, such as nervousness, irritability, emotional instability, depression, headache, nausea, and tension, which occur premenstrually and which usually subside at, or shortly after, the onset of menstruation. They may last as long as the second half of the menstrual cycle and sometimes produce frank psychiatric disturbances. Relief, lasting for many months, is claimed after treatment with testosterone propionate by several authors (see review by Carter, Cohen and Shorr). Hemisrania, appearing before menstruation and disappearing during gravidity, are influenced by progesterone, given several days before menstruation.

Rappaport (1948), Baruk *et al.* (1948), Klotz and Borenstein (1949) investigated hyperfunction of the follicular system of the ovary, resulting in hyperfolliculinaemia, and its consequences on psychic symptoms and mental disorders. Electro-shock is generally ineffective in mental disorders due to hyperfolliculinaemia. Testosterone treatment is sometimes effective. An extensive investigation of the menstrual cycle and psychosis has been published by the German gynaecologist, Knaus (1948). He carried out, on the basis of his own scheme, a careful analysis of the periodicity of acute psychotic disturbances in a schizophrenic woman and co-ordinated it with the menstrual periods during a year. At each period a remission of the schizophrenic symptoms was seen. This patient was unsuccessfully treated 30 times with electro-shock and with oestrone. She then received a blood transfusion of 420

ml. of blood from a five-months pregnant woman, started to recover on the next day, and did not show any psychotic disturbances for the next two years. The blood transfused contained 20/40,000 units of chorionic gonadotrophin, which, according to Knaus, was responsible for the therapeutic result.

Carter, Cohen and Shorr (1947) review the patho-physiology of the female libido. It seems established at present that the most effective treatment for frigidity is testosterone. This action is not yet understood. Apart from its well-known effect on the external genitalia, its influence on steroid hormone metabolism and possibly brain function may be of consequence.

According to Hamilton *et al.* (1945) and Heller and Myers (1944), sharp rises of gonadotrophic hormone excretion occur after castration. Male climacterics, according to Heller and Maddock (1947), excrete gonadotrophic hormone identically with the surgical castrate. The authors claim that, in contrast, in normal or neurotic ageing men urinary gonadotrophins are not elevated. Heller and Maddock studied 23 cases of male climacteric, who all had high gonadotrophin excretion and symptoms similar to the female menopause, and impotence. In eight cases testicular biopsy showed abnormalities of the Leydig cells. Heller and Myers have discussed further the controversies about the male climacteric. Their view, that "whereas in the female menopause is an invariable and physiological accompaniment of the ageing process, in the male the climacteric is an infrequent and pathological accompaniment of the ageing process," seems well founded. Simpson (1950) concludes that the male climacteric is physiological, although a complete syndrome is relatively rare, and that it tends to occur rather later than the female menopause, and to continue for a decade or more.

The menopause-like symptoms are obviously androgen-deficiency symptoms. Testosterone therapy relieves both the physical and the psychic symptoms, of the male climacteric.

Heller and Maddock (1947), Simpson (1950), Walker and Strauss (1948), and Strauss, 1950) have reviewed impotence. Simpson (1950) claims that cases of psychological impotence outnumber organic impotence by about ten to one. He distinguishes also another type where psychological impotence occurs in the course of endocrine disease. Simpson recommends in doubtful cases an assay of urinary gonadotrophins, which are usually raised in impotence of gonadal origin. Heller and Myers (1944) distinguish psychogenic impotence from impotence due to overt testicular failure by urinary gonadotrophin assays. All these authors agree that psychogenic impotence does not respond to testosterone therapy, which is usually effective in hypogonadal failure.

A broad neuro-endocrinological concept indicates that these differentiations are by no means as clear-cut as they at first appear. Psychological impotence, for instance, might represent a psychological trauma which in its turn inhibits or stimulates the pituitary function, producing endocrine disturbances of different kinds. Psychological impotence might in this way initiate a neuro-endocrine and psychopathological vicious circle, as might organic impotence.

The aetiology of homosexuality is still very doubtful. Endocrine imbalance, changed oestrogen-androgen ratio, psychogenic maladjustments, and influence of the environment in determining the direction of the sex drive are the main

hearings of this discussion. No single author has, in his conclusions, taken into account all the factors concerned. The endocrinologist, relying on the experiences of the animal experiments that female sex hormone produces female sex drive, and male sex hormone male libido, is apt to ignore the fact that analogies from animal experiments to human behaviour cannot be drawn. Possibly the greater degree of differentiation and development of the frontal part of the human brain influence the direction and development of sex drive. It should not be forgotten, on the other hand, that without the primary production of sex hormones, no sex drive at all can develop. Heller and Maddock, in their recent review (1947) about homosexuality, came to the conclusion that the power of the human sex drive is largely dependent on physiological factors, i.e. proportional to the amount of circulating androgen (or oestrogen in the female). On the other hand, the direction of the human sex drive seems to be largely dependent upon psychological factors, which are conditioned by the early environment and sexual experiences of the individual.

It is clear that androgenic treatment only tends to increase the power of the sex drive in normal and homosexual males, but cannot influence the direction of the sex drive. Castration can diminish the sex drive, but will not change its direction in normal or homosexual. These conclusions are in agreement with investigations carried out by various workers in recent years, and with our personal experience.

Golla and Hodge (1949) have recommended high doses of oestrogen for the treatment of male homosexuals, apparently to suppress the libido. This treatment may, however, operate through continuous suppression of the pituitary anterior lobe function (which is not without danger), since it is known from animal experiments that the first symptom seen in rats after hypophysectomy is cessation of any sex drive.

There is still much work to be done on the androgen-oestrogen ratio in homosexuals, which has frequently been claimed to be abnormal in certain types.

It may be that the lower the intellectual level the more closely does the effect of male or female sex hormones on the sexual drive approximate to that observed in animals; thus, in samples from humans of superior intelligence, intellectuals or creative artists, the importance of alterations in the hormone equilibrium is probably of a totally different order from that in dullards.

It is very questionable whether a separation between force of sex drive and its direction is valid for individuals of all constitutions, dispositions, and especially levels of intelligence.

Hoskins and Pincus (1949) compare the androgen and oestrogen ratio of 23 normal men, 11 normal women, and 29 schizophrenic men. There was considerable overlapping in the various categories, but the women excreted more oestrogen and less androgen than did the men. The total oestrogen output of the patients was lower than that of the women, but significantly higher than that of the normal men. The androgen output of the patients was higher than that of the women, but significantly below that of the normal men. The mean androgen-oestrogen ratio in the women was 2.3, in the men 16.3, and in the patients 9.7.

In animal work one may cite only that psychic oestrus was exhibited by golden hamsters one to two hours after injection of desoxycorticosterone acetate (Isaacson, 1949), and was also seen after administration of progesterone via the lateral brain ventricle (Kent, 1949).

STEROID HORMONES.

The steroid hormones are dealt with here under a separate heading, since their metabolism and production has become an extremely complex problem, implicating various organs—adrenal cortex, gonads, liver, brain. It was found recently by Gordon *et al.* (1950) that the concentration of ketosteroid-like substances in the brain is higher than in the testicles, and that their concentration is decreased after castration, but increased after epinephrectomy. The influence of steroid substances on the brain function and the role played by the brain in the steroid metabolism is still obscure. The liver plays an important role in steroid metabolism. Oestrone perfused through the liver or incubated with liver suspensions is rapidly inactivated, as is testosterone; but kidney metabolizes testosterone, the final products apparently being 17-ketosteroids. The metabolism of oestrogens was recently reviewed by Heard and Saffran (1949) and Segaloff (1949), the metabolism of androgens by Samuels (1949).

These facts are mentioned to illustrate the complexity of the problem. At present steroid metabolism in mental patients can only be estimated by studying the excretion of different steroid substances, but it is unwise to draw conclusions about metabolic and endocrine processes in the body from the results obtained.

Female patients suffering from liver damage frequently have menstrual disturbances, even when the ovary function is primarily intact. It is, therefore, understandable that primary liver disturbances, directly, or secondarily—via disturbed gonadal function—may influence the psychic pattern.

It is, of course, unknown to what extent this represents an interference with the influence of the liver on steroid metabolism. Lingjaerde *et al.* (1949) found normal excretion in most schizophrenics investigated. Some of the figures are extraordinarily low, especially for schizophrenics in the active phase and those in a marked stuporous state. These findings agree with the experiences of the present authors. Ketosteroid values above normal are also seen in some cases of schizophrenia. It is important that the excretion rate of urinary 17-ketosteroids, estimated at intervals for several months, showed constant or widely varying values. In some patients the ketosteroid excretion during the course of a year varied between 4 and 26 mgm. per 24 hours (Reiss *et al.*, 1949). Variations in 17-ketosteroid excretion during day and night were investigated in normal individuals by Pincus (1947), who reported minimal excretion during sleep, a tendency to maximal values during the hours shortly after waking, and a regular decline during the hours of the day. Hemphill *et al.* (1949) and Reiss found such a normal pattern in only a few of the psychotic patients investigated. The majority of their patients showed a greatly enhanced increase in the "waking" output, or the

maximum excretion occurred for several hours daily, or very slight variations would be seen during the day. In another group there was a second peak in output, occurring later in the day, in addition to the morning peak. Catatonic patients showed very little change in the diurnal pattern and a much flatter curve of the ketosteroid excretion measured over several months; restless and acutely hallucinated patients showed much sharper changes in the diurnal pattern, several times as great as the normal subjects, and in these there were much greater variations in the daily output. Particularly instructive were the recorded excretions of ketosteroids and cortins of a typical manic-depressive patient, with relatively short-phase cycles. Several cycles were fully investigated in the course of a year and it was found that levels ranged between 2 and 18 mgm./24 hours. Changes of 100 per cent. to 300 per cent. occurred in as short a period as ten days. The cortin excretion changed during each cycle by over 100 per cent., as also did that of 3 (β)-hydroxy-17-ketosteroids. There was an inverse relationship between changes in beta-steroids and cortin excretion. A similar inverse relationship between beta-steroid excretion and oestrone excretion was sometimes noted. The onset of the depression was accompanied by a tendency to excretion of a high proportion of beta-steroids and low cortin. Cortin excretion was usually rising at the transition into mania, when, at the same time, the proportion of beta-steroids was falling.

The diurnal variation of 17-ketosteroid excretion is an expression of the adaptation by the individual to the demands of his environment in daily life. Very little adrenocortical activity is necessary during sleep, and the greatest demand in the 24-hour cycle is in the process of waking. It is, therefore, understandable that the excretion is at a maximum for normal subjects during the first few hours of the morning—an adaptation mechanism evidently disturbed in schizophrenics.

Systematic investigations on schizophrenic patients have shown great variations, not only in the total 17-ketosteroids, but also in the ratio between alpha- and beta-ketosteroids excreted. The investigations on the manic-depressive patient mentioned above have already pointed to a possible relation between depressive states and increased beta-ketosteroid excretion. Testosterone treatment of certain psychotic patients reduces the excretion of alpha-ketosteroids when there is therapeutic success (Reiss, 1949), and the converse may be true. Injection of the beta-ketosteroid dehydroisoandrosterone produced in some psychotic patients a marked rise in the excretion of the 3-alpha-hydroxy-17-ketosteroids, and sometimes increases of cortin and oestrogens. A typical chronic deteriorated schizophrenic, hospitalized for 14 years, had a complete remission and was discharged from hospital to productive employment after treatment on these lines with dehydroandrosterone (Reiss *et al.*, 1949). Hoagland (1944) reported improvement in work efficiency after administration of pregn-5-en-3-ol-20-one.

PITUITARY.

Carbohydrate metabolism of brain increases after hypophysectomy, shown by measurement of hexokinase (Reiss and Rees, 1947.) Anaerobic glyco-

lysis also increases and can be restored to normal by treatment of the animals with adrenocorticotrophic hormone. Investigation of phosphorylation, using P^{32} , shows that phosphorylation in the acid-soluble fraction increases and can be reduced by adrenocorticotrophic hormone. These investigations suggest an origin for mental accompaniments of disturbed pituitary function. (Reiss *et al.*, 1949.)

Torda and Wolff (1949) found that neuromuscular fatigue occurred in hypophysectomized animals, and is due to both a moderate dysfunction of the muscle and a marked dysfunction of the nerve element (either nerve or myoneural junction).

Fortier and Selye (1949) report that adrenocorticotrophin released from the pituitary by cold or surgical trauma is not affected by severance of the hypothalamo-hypophyseal connection. This result agrees with the claims made by Harris (see above) about brain-pituitary connections.

Benda (1947) defines the mongoloid as "a pituitary cretin." According to him, mongolism is congenital hypopituitarism, comparable to cretinism, which is congenital hypothyroidism.

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INTELLIGENCE TESTING.

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I. INTRODUCTION.

IN the last few years investigation of psychiatric problems by means of mental tests has been pursued on an unprecedented scale. There have appeared a vast number of papers (scattered in a bewildering variety of journals) and not a few books, some of forbidding size, all, according to one or other reviewer, "indispensable." One reason for this plethora is that the war, by focussing attention on matters apt for psychometric investigation, such as personnel selection and the effects of head injury, presented psychologists with golden opportunities which were avidly seized. The most important reason, however, is that psychologists have greatly developed and extended their techniques and their sphere of activities.

The I.Q., at best a crude and often misleading measure of global intellectual performance, is no longer a subject of much interest. Now, separate aspects of cognitive functioning are reported on independently, and stress is laid not so much on scores themselves, but on the relation of scores to one another, i.e. the psychometric pattern. Many attempts have been made to define the different patterns in different diagnostic groups and to study the light thrown by a patient's pattern on his illness.

The departure from mere I.Q. measurement is further reflected in the increased use of tests of the type popularized by Goldstein—tests of ability to sort and abstract—in which the quality of the performance rather than the level reached is the subject of study. Such tests are not administered with a rigidly standardized technique, but are varied by the tester according to the patient's responses in order to bring out the special characteristics of his cognition. This calls not only for ingenuity on the part of the tester, but in addition, wide experience and deep psychological understanding of the patient. More and more, the familiar standardized intelligence tests, such as the Terman-Merrill and Wechsler Bellevue, are being studied from these qualitative rather than from the quantitative aspects.

There is, too, growing recognition that what is tested even with so-called tests of intelligence is not the subject's intellectual functions isolated from the rest of his personality, but the person as a whole. Wechsler (1943) argues that the "residual variability" found in statistical studies is due to non-intellectual factors in intelligence and that scales should be designed to take these into account. Hanfmann (1944) believes that future investigations will uncover qualitative variations within the range of normal intellectual performance

which reflect significant differences in the underlying personality patterns. Hunt (1946), Wladowsky (1946) and Schafer (1946, 1948*b*) are among the many who stress similar points. Thus, intelligence testing has now become a supple and flexible art, whose adherents claim not only to measure intelligence, but also to be able to help the psychiatrist at many points; in differential diagnosis (for example, Reichard and Schafer, 1943; Wladowsky, 1946; Schafer, 1946; Aita, 1946, 1947; Kogan, 1946; Rashkis, 1947*a*, etc.), in planning treatment (e.g. Schnack, *et al.*, 1945) and in assessing the results of treatment (e.g. Babcock, 1947; Porteus, 1944, 1947; Rylander, 1946, 1947).

Still more important progress has been made in the use of non-intellectual tests, particularly projection tests. According to Louttit and Browne (1947) the T.A.T. and Rorschach are among the five tests now in most common use, the others being the Stanford-Binet, Wechsler and Goodenough. They state that since 1935 the trend has been towards greater and greater use of such tests. There has, too, been a revival of interest in tests of conation and motor performance. The clinical psychologist to-day employs a great variety of techniques well illustrated by Shakow *et al.* (1945), whose battery of tests includes the Stanford-Binet or Wechsler Bellevue, Rorschach and T.A.T., each of which may consume an hour or more. A detailed picture of how the modern clinical psychologist operates is given by Schafer (1948*b*).

Clinical psychology is passing further from the stage of collecting data into the stage of systematization and formulation of theory (Rapaport, 1947*b*). Psychologists are not content merely to state that in such and such a condition, such and such test results are obtained. They are boldly deducing from these results opinions on the underlying psychopathology. Goldstein has for many years discussed the psychopathology of organic dementia in the light of special test performance, and he has extended his ideas to schizophrenia. He has been followed by Aita (1946), Lynn *et al.* (1945), Allen (1947, 1948) and others in the first of these fields, and notably by Rapaport and his colleagues at the Menninger Clinic in the second. Babcock reiterates (1944, 1945, 1947) her belief that in neuroticism, the test performance reflects the fundamental type of mental efficiency (or inefficiency) from which the illness derives rather than that the test results derive from the illness.

There is even a tendency to depose other methods in favour of psychometric methods of diagnosis. For example, according to Menninger *et al.* (1947), "Psychological testing has revealed the presence of a schizophrenic process in many patients, while clinical evidence of schizophrenic tendencies is faint or absent. To put it another way, the psychologist is discovering schizophrenia or 'potential' schizophrenia or 'latent' schizophrenia in patients who are not suspected of being classifiable as schizophrenic according to old concepts. . . . This is not happening in a few cases, but in a considerable number of cases, enough to make us suspect that the vast majority of persons in whom a 'schizophrenic process' is present are not easily recognizable as such without specific testing."

Some psychologists openly challenge common psychiatric practice. Following up views expressed by Schafer and Rapaport (1944), Rapaport (1948) states: "We should not altogether naively accept current psychiatric nosology.

Our job is to contribute by our explorations to nosological clarification and if necessary to the crystallization of new nosological entities." With regard to screening the maladjusted, Zubin (1948) says, "Furthermore, the accepted psychological and psychiatric diagnostic categories are not too helpful. Perhaps new goals will have to be established; not diagnostic goals, but therapeutic goals." Wells (1946), too, says that the proper aim of the analysis of psychometric ability is to lead to an "understanding of the case in terms of what to do about it, which is more than capable of by-passing the diagnostic label altogether." In a cheerful onslaught on psychiatrists (and other psychologists), Babcock (1945) states "that the fundamental error of psychiatry is its lack of a broad education in theoretical and practical aspects of the field in which it practices: that of individual psychology." She contrasts the barrenness of psychiatry with the "achievements in scientific psychology," those cited, incidentally, being her own.

No one can justifiably criticise these developments in principle. Psychologists are approaching psychiatric material with new techniques and they are fully entitled to form new concepts and classifications on the basis of the data they elicit. We must, however, draw attention to the disagreements that exist amongst psychologists themselves (see section V), and it seems to us that many recent papers exhibit a tendency to generalize prematurely and too far on unconfirmed results.

Naturally, the functions and status of the clinical psychologist have been studied. According to Wittman (1944), the work of a psychologist in a mental hospital falls into four categories: (1) routine psychometrics, (2) interpretation and analysis of test results in order to lead to a better understanding of the patient, (3) research, (4) teaching. A "well organized and psychometric routine" is remarkably full. It includes an initial evaluation of co-operation and behaviour; evaluation of test reaction with a view to more detailed personality testing; checking of the initial psychometric evaluation with further tests for specific points, e.g. deterioration; objective evaluation of therapy by means of tests before and after; evaluation of the effects of hospitalization, and testing for the purpose of vocational guidance. The psychologist is also called on in the selection, "placement, promotion or transfer" of the staff. Wright (1948) and Cheyney and Strongin (1946) express similar views. It is not surprising that the latter calculate that for each 300 patients there are needed a "chief psychologist, an assistant psychologist and two interns." Other papers relevant to the present status and future of psychological testing have been published by Rapaport (1947*b*, 1948), Menninger *et al.* (1947), Schafer (1948*a*) and Zubin (1948).

In spite of the voluminous literature, there are few introductions to clinical psychology suitable for the psychologist ignorant of psychiatry or the psychiatrist ignorant of techniques.*

As has been indicated above, clinical psychology now comprises far more than intellectual testing. The rest of this chapter, however, will be devoted

* Pennington and Berg's book (1948) had not been seen by the author at the time of his death. A review by him of Pichot's *Les Tests Mentaux en Psychiatrie* appeared in the *Journal of Mental Science*, for April, 1950.—EDS.]

to cognitive testing, other matters being considered elsewhere by Eysenck. Excellent reviews of work up to the time of publications are to be found in Hunt and Cofer (1944), and Rapaport *et al.* (1945). Simon's historical review (1943) is interesting but not detailed. Reviews of investigations by means of the Wechsler Bellevue Scale have been published by Rabin (1945*b*) and Watson (1946). Attention is drawn to the yearly reviews published by the *American Journal of Psychiatry*.

II. TECHNIQUES.

It is impossible to mention individually the countless techniques that have been described in the last few years. General reviews of those devised for use in the selection of Allied Services' Personnel are given by Vernon (1947), Hunt and Stevenson (1946) and in many papers published in the *Psychological Bulletin*. Other references may be obtained from the invaluable *Psychological Abstracts*. A number of useful techniques are assembled in Wells and Ruesch's *Mental Examiner's Handbook* (1945).

Elgin test reactions scale.—It has long been recognized that the validity of a subject's test performance depends on his co-operation. Wittman's scale (1943) enables the patient's reactions to the test situation to be rated under ten headings.

Measuring intelligence in adults.—Cattell (1943) concludes that it is necessary to agree on what constitutes intelligence before further advance can be made. His is an interesting and important paper, although his conclusion is inconsistent with some modern philosophical views on the nature of measurement. Zuckerman (1946) criticizes the use of M.A.'s with adults. Hebb and Norton (1943, 1944) have devised a verbal comprehension test and a picture anomalies test whose subject matter is designed to appeal to adults, in contrast to the vast majority of tests, whose content is more suitable for children. Guetzkow and Brozek (1947) describe six tests with multiple forms designed for experiments where repeated testing is required.

Scales.—Amongst new scales, the following are likely to become popular: (1) *Army General Classification Test: First Civilian Edition*. Chicago: Science Research Associates, 1947. (2) *Wechsler-Bellevue Intelligence Scale, Form II*. New York: Psychological Corporation, 1946 (referred to and partially described by Altus, 1945, and Aita *et al.*, 1947). (3) Capacity, verbal polarity and orthotude battery (Jastak and Gordon, 1946; Jastak and Stubbs, 1947). These are further discussed in the section on schizophrenia. The battery comprises 12 items, as follows: (1) vocabulary, (2) oral reading, (3) information, (4) analogies, (5) comprehension, (6) digit recall, (7) mental arithmetic, (8) picture anomalies, (9) picture reasoning, (10) symbol substitution, (11) drawing, (12) form boards. Capacity is measured by the mean of the three highest scores, whatever they are, verbal polarity by the deviation from capacity of the mean of the middle three scores on tests (1), (2), (3), (4) and (5), and orthotude by a similar procedure with tests (5), (8), (9), (11) and (12).

Brief tests.—Abbreviations of the Wechsler-Bellevue scale have been proposed by Rabin (1945*b*), Gurvitz (1945), Cummings *et al.* (1946), Kriegman and

Hansen (1947) and Patterson (1948). Various abbreviations of the W.B. scale are compared by Patterson (1948) and by Hunt *et al.* (1948a), who also discuss the Kent revised E.G.Y. test and Thorndike's 15-word vocabulary test. According to Hunt *et al.* (1948) their "C.V.S." scale, composed of the Thorndike vocabulary test mentioned above plus the Wechsler Bellevue Comprehension and Similarities subtests, constitutes a reliable diagnostic measure, acts as an effective screen for mental deficiency, offers a valuable quantitative scatter measure (Vocab. minus C. & S.), and provides good opportunities for exhibiting qualitative aspects of performance. Kent (1945) has published new norms for her emergency battery. Attempting to meet the need for a quick intelligence test capable of being used in everyday clinical practice, Keller *et al.* (1947) describe a battery of only 11 short items, 4 vocabulary, 2 Comprehension, 2 Similarities and Differences, and 3 Arithmetic. Hildreth (1945) assembled from various sources 10 single items, success on any one of which "demonstrates mental ability above the minimum for naval training." According to Pennington (1947), the popular Serial Sevens test "does not appear to measure accurately whatever mental functions are tested by the verbal battery of the Bellevue-Wechsler scale." He finds it unreliable as a measure of intelligence or even as a screen test for mental deficiency.

Memory tests.—Wechsler's scale (1945) for measuring the Memory Quotient (M.Q.) contains the following items: Personal and Current Information, Orientation, Mental Control (e.g. 20-1), Paragraph Memory, Digits, Designs from Memory, and Paired Associates. Benton (1945) has published an extended form of the Designs from Memory test. It should be noted that Eysenck and Halstead (1945), who factorially analysed the above or very similar tests, could find evidence of no separate memory factor. The only factor that emerged seemed to be identical with g. Feldman and Cameron (1944) describe two very simple methods of measuring memory in severely demented patients: (1) To note the highest given number to which the patient can count without forgetting the given number; (2) to note the length of the time the patient can spell three-letter words without forgetting an initially given 3-digit number.

Deterioration tests.—Bradford (1945) draws attention to factors which tend to invalidate the score on the vocabulary half of the Shipley Hartford scale. He proposes a shortened verbally administered form. A method of assessing the degree of abnormality of scores on this scale was devised by Slater (1945). Wechsler's Deterioration Index (1943) is calculated by the formula, *Hold—Don't Hold*. The "Hold" items are Comprehension or Vocabulary, Information, Picture Completion and Object Assembly, the "Don't Hold" being Digits, Arithmetic, Digit Symbol and Block Design. The Hunt-Minnesota Test (Hunt, 1943, 1944a and b), depends on the discrepancy between score on vocabulary and on learning and recall of Designs and Paired Associates. Hayman (1943) used the Serial Sevens test, Goldfarb (1946) and Grassi (1947), modified Kohs' Blocks tests. Halstead's "Impairment Index" (1947) is of research rather than clinical interest, since many of the items require elaborate laboratory equipment.

Miscellaneous.—Rey (1941) and Osterieth (1944) have experimented with a complex design which may be used for the measurement of intelligence and

for the detection of memory defects and intellectual impairment. New sorting tests have been published by Berg (1948) and Brody (1948).

III. MENTAL DEFICIENCY.

It is possible that the publication in full of the results of testing in the Services will throw new light on the psychometric criteria of ability or inability to lead a socially useful life. The success of the Pioneer Corps may eventually lead to important developments in the organization of border-line defectives, and consequently to some revision of concepts about the significance of low I.Q.'s. A low I.Q. has, of course, never been accepted on its own as proof of deficiency. It has to be checked by examination of the patient's life-history and by all the available evidence about his personality and emotional control. Sarason and Sarason (1945) illustrate the use of projection tests in this connection. Methods of detecting malingerers of mental deficiency are described by Hunt and Older (1943) and Goldstein (1945).

Terman-Merrill pattern.—The test patterns of mental defectives on the Terman-Merrill have been studied by Sloan and Cutts (1947) and by Thompson and Magaret (1947). The lists of "hard" and "easy" items given in both papers are very similar. According to Sloan and Cutts, Verbal Absurdities, Sentence Memory and Opposite Analogies account for 10 of the 15 "hard" items, and the other 5 are of a similar nature. The easy items are more concrete, or if verbal, do not require manipulation of abstract concepts. Thompson and Magaret suggest three possible hypotheses: (1) That the easy items involve practical experience; (2) that the hard items demand freedom from intrapersonal rigidity.

Verbal/Non-verbal Pattern.—Interest continues in the relation of verbal to non-verbal test scores as an indicator of social adjustment. Although Weider *et al.* (1943) report that children with behaviour disorders do well on non-verbal items, Jastak and Allen (1944) and the Sarasons (1946) find that high performance ability relative to verbal ability is a characteristic of better adjusted groups. Porteus (1945) reports poor qualitative performance on his Maze test in delinquents and socially maladjusted defectives. Wallin and Hultsch (1944) believe, on the other hand, that a Performance > Verbal pattern has little significance, and maintained that "short cuts to diagnosis in the field of psychology and psychiatry have usually proved to be will-o'-the-wisps, intriguing but deceptive." Performance on the McGill Picture Anomalies and Verbal Absurdities also failed to distinguish between well and badly adjusted institutionalized defectives (Sloan and Oblinger, 1947).

I.Q. changes.—Kaplan (1943) reapplied the 1916 Stanford-Binet test to 66 morons after an average interval of nearly 15 years. The average decline was only 6.65 M.A. months, which is, in fact, less than the normal decrement with advancing age allowed for in Wechsler's scale. The average age and average I.Q. at the first test were 41.17 years and 57.01 respectively. There were no marked differences in the findings when the cases were treated separately according to sex, age at first test, interval of less or more than 12 years, and initial I.Q. above or below 60. Nine patients increased their score. There was a mean loss of only 0.9 I.Q. points over a mean interval of 10.61 years in 56

merons tested by Sloan (1947). These 56 were part of a larger group of 80 morons with a mean I.Q. of 58.47 and a mean C.A. of 22.49. As many as 2,267 test-retest pairs with a mean initial I.Q. of 50 and a mean initial C.A. of 14.8 were studied by Sloan and Harman (1947). Amongst those over 5.5 years, 31 per cent. gained in I.Q. and 61 per cent. lost, with a mean loss of 2.6 I.Q. points. This rather faster rate of loss stands in greater contrast to the other reports because the subjects were, on the whole, younger. Unfortunately, Wechsler's Deterioration Index cannot be used to follow the changes in mental defectives, because Sloan (1947), Johnson (1947) and Boehm and Sarason (1947) all found positive deterioration indices in undeteriorated defectives, amongst whom low scoring on the "Don't Hold" tests seems to be a lifelong characteristic.

Brain-injured defectives.—A most interesting series of papers, based on the results of special tests, have been published by Strauss, Werner and collaborators (see Strauss and Lehtinen, 1947). In general they find in brain-injured defectives, to a far greater extent than in non-brain-injured defectives, qualities of behaviour such as are described by Goldstein in brain-injured adults. The Sarasons, however (1947), distinguish two groups amongst cerebral palsied defective children; one in which the Terman score was less than the Kohs', and in which the Rorschach and the EEG were relatively normal; the other in which the Terman score exceeded the Kohs', and the Rorschach and EEG were abnormal. In the first group it is claimed that the pathological disturbance is subcortical rather than cortical.

IV. ORGANIC SYNDROMES.

Deterioration tests.—The current popularity of deterioration tests as methods of diagnosing organic impairment calls for an examination of their utility. Shakow (1946) writes: "While the 'vocabulary-other tests' comparison may be useful in disclosing qualitatively the presence or absence of impairment, the wisdom of employing it as a quantitative index of degree of impairment is called into question by the finding in this study (of schizophrenics) that there is no relationship between the size of the 'vocabulary-other tests' discrepancy and the degree of impairment as judged by careful clinical estimate." Rabin's (1944b) results with more varied patients, including luetics, led him to the same conclusion. Although all his psychopathological groups showed I.Q. discrepancies in favour of vocabulary, "little difference is to be noted between the several diagnostic groups." Schafer (1944) found that "57 per cent. of 41 schizophrenics had Babcock efficiency scores well below the norm associated with their vocabulary level." Rabin (1947a) repeated earlier observations that the "vocabulary-other test" discrepancy rises with increasing age irrespective of the mental condition.

The unreliability and nonspecificity suggested above appears to apply to other deterioration tests. Amongst 977 neuropsychiatric patients tested by Wright (1946) with the Shipley Hartford Test, only 38 per cent. had normal scores, although it is inconceivable that all the remainder had organic impairment. Cole *et al.* (1947) found pathological Hunt-Minnesota indices in 39

per cent. of a mixed group, none of whom had organic cerebral disease. Pathological scores on this test for organic brain damage were found by Meehl and Jeffery (1946) in about half their cases of functional depression, while Malamud (1946) found pathological scores in 55 per cent. of normal persons. Juckem and Wold (1948) show that only negative significance can be attached to this test in persons with superior vocabulary levels. Impairment was shown by only 50 per cent. of the brain-damaged patients tested by Graham and Kendall (1946) with a designs from memory test.

Wechsler's Deterioration Index has also been criticized (McNemar, 1945). There is even disagreement about which tests "Hold" and which "Don't Hold." Contrary to Wechsler's views (*vide supra*) Rabin (1945*a*) includes in the former group Similarities and omits Object Assembly and Picture Completion, while in the latter group he includes Picture Completion and omits Digit and Arithmetic. Allen (1948*a*) reports that Object Assembly is much affected in brain-injured patients, of whom only 54 per cent. had pathological indices calculated according to Wechsler's formula. Tooth (1947) was unable to differentiate between neurotic and organically deteriorated patients by means of the test, and Olch (1948) avers that normal advancing age produces similar effects to the schizophrenic process on approximately half the subtests of the Scale. The failure of the index to distinguish between deterioration and deficiency has already been mentioned. Garfield and Fry (1948) find little relationship between Wechsler Deterioration Indices and Shipley Deterioration Quotients. Ruesch and Bowman (1945), indeed, doubt the reliability of any psychometric diagnosis of organic intellectual deterioration.

Nevertheless, Aita *et al.* (1947) believe that Wechsler's scale has "definite diagnostic value in the determination of brain injury" and they found it to be superior in this respect to both the Shipley-Hartford and Hunt-Minnesota tests. Reynell (1944) states that an index based on the comparison of Vocabulary, Information and Comprehension scores with Arithmetic, Digits and Similarities scores, gives a reliable diagnosis in 80 per cent. of cases of head injury. Amongst patients with traumatic or other cerebral pathology, clinical and Wechsler psychometric diagnosis coincided in 72 per cent. of cases examined by Greenblatt *et al.* (1946), while Goldman *et al.* (1946) reported only 18 per cent. false positives. Levi *et al.* (1945) illustrate with approval the use of the Wechsler index in clinical practice. The absence of a large "vocabulary-other test" discrepancy is taken by Delay *et al.* (1947) as reliable evidence of the absence of deterioration.

It appears to us that the position is justly summarized by Johnson and Lassner (1945) who, writing of the Worcester Wells Memory Test, state: "A subnormal score may be the result of low intelligence, of schizophrenic or allied preoccupations of various kinds, of melancholic retardation, of dreamy and clouded states, and, in short, a variety of widely diverse psychiatric conditions, all of which interfere with maximal and sustained attention. Therefore, caution should be exercised with this test as with all so-called 'deterioration' tests in interpreting subnormal results, as a low score may result from global configurations of a nature quite different from organic deterioration. However, assuming proper test conditions with sustained and maximal attention, normal

or better than normal scores can definitely be interpreted as ruling out deterioration, whereas subnormal scores provide a rough quantitative index of the degree of impairment."

Senility.—The psychometric pattern of normal old persons is important, since it is only in relation to this that the significance of the pattern in senile dementia can be evaluated. The comparative preservation of vocabulary ability has again been stressed by Halstead (1943), Rabin (1944*b*, 1947*a*) and Fox (1947). Thorndike and Gallup (1944), however, found a drop after the age of 60 corresponding to 8–10 M.A. months as compared with the performance of subjects aged 20–29. A carefully planned comparison by Sward (1945) of the performance of persons aged 60–80 who had held high academic posts with that of persons aged 25–35 holding similar academic posts revealed few significant differences except in the speed of reaction on unfamiliar tasks. Since this older group was very intelligent, it must be remembered that deterioration has been found to occur less and later the higher the initial intellectual level. In more average groups investigated by Fouldes and Raven (1948), decline was found to set in at about age 30, becoming faster after age 50. Halstead (1943) intensively studied a group of old persons aged 68–83. Their M.A. was estimated to be about M.A. 10–11. He gives interesting lists of the items found by these aged subjects to be most difficult, moderately difficult, and least difficult. His conclusions are in line with earlier workers, namely, that the tasks simplest for them involve old mental habits, while the most difficult require the ability to break away from old mental habits. Wechsler's views (1943), with which Wittman (1943) is in general agreement, are implied by the fact that his scale allows for a decrement of 6 M.A. months per decade. His deterioration pattern of "Hold" and "Don't Hold" tests has already been mentioned. A useful summary on mental decline and its retardation has been published by Lawton (1945).

Senile dementia.—Although demented senile patients may be able to define words, Ackelsberg (1944) shows that they lose the ability to use words in proportion to the degree of dementia. Thus synonym, antonym, categorization, homograph and word-naming tests can all be used as valid indicators of deterioration. The similarity of her results to those of an earlier study of epileptics by Capps, "gives strength to the idea that the course of deterioration in epilepsy resembles that in senile dementia." Halstead (1944) found a median M.A. of 7 in a group of senile demented on the same tests on which his group of more normal old persons scored a M.A. of 10–11. Two of his interesting tables are reproduced (Tables I and II).

Memory defects have been studied by Cameron (1943) and Meyrat (1944). The former believes that the "disorders in the early stages of retention so frequently found in the aged exert a widespread influence on the total behaviour of the individual," and that reliance is often placed by the aged on compensatory mechanisms such as "the use of happenings in the environment as cues for information as to what activity (the subject) is engaged upon." Meyrat investigated the reproduction of various activities after intervals up to five minutes. There was not always a parallel between ability to do a thing and to recall what was done, nor between the degree of impairment and age or duration

TABLE I.—*Discriminatory Value of 25 Tests Between Groups of "Less and More Demented" Senile Patients (after Halstead, 1944).**Good Discrimination.*

Picture Memory.
 Reading Speed.
 Digits, Forward and Reversed.
 Colour Naming, Reversed.
 Recall of Paragraph; immediate delayed.
 Naming Months, Reversed.

Fair Discrimination.

Block Designs (Kent).
 Vocabulary.
 Knox Cubes.
 Naming Birds.
 Arithmetic.
 Porteus Mazes.
 Recognizing Photographs.
 Sentence Memory.

Poor Discrimination.

Naming Months.
 Naming Colours.
 Tapping.
 Naming Animals.
 Tracing Tests (2).
 Writing Tests (2).
 Packing Cubes in Box.

TABLE II.—*Approximate Mental Ages of "More Demented" Senile Patients on 13 Tests (after Halstead, 1944).*

Test.	Mental age.
Vocabulary	10.5
Naming Months	9.5
Arithmetic	8.0
Reading Words	7.0
Repeating Digits, Forward	7.0
" " Backward	7.0
Sentence Memory, rote	7.0
Knox Cubes	6.5
Block Designs, easy series	6.0
Naming Months, Backward	5.0
Recall of Paragraph, immediate	5.0
" " delayed	5.0
Porteus Mazes	5.0
Average mental age, 13 tests	6.8

of symptoms. In senile dementia memory is affected patchily, not as a whole, and generally less than in Alzheimer's disease.

The quality of performance on the Goldstein-Scheerer Object Sorting test and the Wechsler-Bellevue scale, was found by Cleveland and Dysinger (1944) to be similar in senile and schizophrenic patients. Although members of both groups were able to respond to verbal items on an apparently abstract level, they could sort objects only on a concrete level. Eysenck (1945) reports that the type of errors made by demented subjects on a board form of the Matrices test is not different from that of normals of the same mental age (about M. A. 8).

Head injury.—Ruesch and collaborators have investigated intellectual functions in relation to consciousness in the early and late post-traumatic stages. On the basis of the responses to Serial Sevens, Digit Span, Visual Span for Objects, Pictorial Similarities and Absurdities tests, repeated several times within the first few days after recovery of consciousness, the conclusion was reached that ability to sustain effort was most affected. Improvement follows more quickly in accuracy than in speed. Ruesch and Moore (1943) declare that "the disturbance of consciousness after injury to the head can be measured by the ability to submit to testing," and such tests are included by Ruesch and Cobb (1943) in a scale for measuring disturbance of consciousness. From a study of the later effects of head injury, Ruesch (1944) drew these conclusions: "The following tests measured the impairment best: 100-7 test, Pictorial Absurdities, Hole-in-the-Board test, Pictorial Discrimination, Naming of Colours, and Reading. The mental functions affected are primarily speed, judgment, and ability to keep up a sustained effort. About one-half of all subjects suffering from head injury show slight intellectual defects. These become less marked with increasing remoteness from the time of the injury. If the impairment is reversible, the duration is usually a matter of less than three months. The impairment seems to be related to the severity of the brain damage. The more serious the intellectual defect, the higher is the incidence of abnormal neurological signs." The similarity of the early and late effects of head injury is apparent. Cole (1945) also has established that the degree of chronic impairment correlates closely with the degree of immediate impairment of intellectual ability. Ruesch (1945) made the interesting observation that after head injury subjects above average intelligence had lower O_2 consumption, heat production and B.M.R. than less intelligent subjects, although the significance of this is not clear.

The Wechsler Bellevue scale was used by Goldman *et al.* (1946), who state, "As a rule, performance on non-verbal items (Picture Arrangement, Picture Completion and Block Design) is most markedly affected, but there is always at least one verbal subtest on which there is also loss of ability to function." Further reports on what seem to be the same patients are presented by Greenblatt *et al.* (1945, 1946). Reynell's index (*vide supra*) based on the Wechsler Bellevue pattern of 520 cases, implies that three verbal items, Digits, Arithmetic and Similarities, are affected. Allen (1947, 1948) and Aita *et al.* (1947) report slightly different pictures. Allen's least affected items are Vocabulary, Information and Comprehension (like Reynell's), but his most affected are Digit Symbol, Digit Span, Block Design and Object Assembly. The

five tests most affected according to Aita *et al.* are Arithmetic, Comprehension, Picture Arrangement, Digit Symbol and Block Design.

Zangwill (1943, 1946a) studied memory and learning after head injury by means of repeated sentences and the Rey-Davis Form Board. He found that whereas immediate memory span might be unaffected, learning was usually impaired.

The feature most often noted in the test performance of patients suffering from the effects of head injury is the occurrence of qualitative defects of the type repeatedly described by Goldstein (Halstead, 1945; Frieman and Lemkau, 1946; Aita, 1947; Goldman *et al.*, 1946, etc.). Goldstein himself (1944b) has excellently summarized the consequences of impaired categorical attitude. They occur when the subject "has to do something volitional or intentional; to account for acts to himself; to assume a definite mental act which is not determined by the given situation; to make a choice; to shift reflectively from one aspect of the situation to another; to begin a task and to stop at a certain point voluntarily; to continue an interrupted task; to hold in mind simultaneously various aspects and compare them; to associate common properties reflectively; to plan ahead; to assume an attitude towards the mere possible, to pretend at something; to think and perform symbolically; to detach himself from the outer world or from inner experiences." Greenblatt *et al.* (1945) claim that impairment on abstraction tests is a more useful aid in the diagnosis of brain damage than the EEG. A very detailed account of the examination of a case with the Goldstein technique has been presented by Hanfmann *et al.* (1944).

It is interesting that the test picture in subdural haemorrhage is similar to that found with direct damage to the brain (Abbott *et al.*, 1943; Herman *et al.*, 1944; Wortis *et al.*, 1945). According to the former, successful operation restores the pattern to normal.

Head injury or psychoneurosis? Many attempts have been made to differentiate these two syndromes by means of mental tests. The most exhaustive is reported by Lynn *et al.* (1945), who administered a three-hour battery of tests, including, among others, a test of Simultaneous Concepts, Rorschach, Object Sorting, Thurstone's tests of Primary Abilities and the Wechsler Bellevue scale. The conclusions were: "Rate of new learning and of forming new associations is slow in the late post-concussive patient; the neurotic is sometimes slow, but often as quick as normal subjects. Arithmetic problems and number tasks are likely to be somewhat difficult for the post-concussive patient and easy for the neurotic. Tests involving spatial perception usually elicit good scores in the patient with chronic diffuse brain damage; scores may be normal in patients with anxiety neuroses, but they often make poor scores on these tests. In creative thinking, the post-concussive patient is moderately productive, but more trite and lacking in individuality than the normal. The anxiety neurotic is likely to be unproductive and/or somewhat peculiar in his ideas. In social judgment, general information and emotional control, the post-concussive patient is likely to meet normal standards, whereas the psychoneurotic subject does not maintain a good level of performance. Variability of quality of performance within a single test is likely to be minimal for the

post-concussive patient, but the anxiety neurotic is often eccentric, inconsistent, and unpredictable, with good and poor scores in the same activity. Logical analysis is usually well preserved in the post-concussive patient's approach to tasks, but is frequently supplanted by illogical and impressionistic response in the patient with anxiety neurosis." The frequent use of qualifying adverbs in the above passage provokes the suspicion that lengthy procedures are not necessarily more informative than simpler methods. Tooth (1947), using the verbal half of the Wechsler scale, Kohs' Blocks, and Sorting tests, was unable successfully to differentiate brain-damaged from neurotic patients or from normals, although he believed that the discriminatory powers of sorting tests could be enhanced to a reliable level by taking qualitative aspects into account. Ross and McNaughton (1944) found few features to distinguish post-traumatic and neurotic patients, and made the interesting observation that, contrary to previous reports, even impairment of digit repetition did not differentiate the groups. There was no significant correlation in his subjects between pathological Shipley-Hartford scores and signs of brain damage elicited with either the pneumo- or electro-encephalograph. Zangwill (1943, 1946a) observed similar quantitative changes on learning and memory tests in both types of patients, but believed that the brain-damaged persons exhibited distinctive perseveration of wrong responses. Memory for designs also fails to distinguish the groups, for Graham and Kendall (1946) found that only 50 per cent. of head-injured patients showed impairment, although it must be admitted that very low scores were made only by organic cases. None of these authors pay much attention to what seems to us an important point which may account for some of the failure to distinguish post-traumatic and neurotic patients—namely, that the post-traumatic patient often has, in addition, a neurotic reaction to his defects.

Qualitative aspects.—As in other diagnostic groups, much attention has been paid to the qualitative aspects of test performance. Porteus (1945) claims that when his Maze test is scored qualitatively, good differentiation is obtained between normals and persons with various types of instability or psychopathy. Zangwill (1946a) finds that errors of neurotic patients on the Rey-Davis Board are uneven, but lack the characteristic perseveration of those of organic patients. Lewinski (1945a and b) and Tooth (1947) are among others who mention the diagnostic importance of qualitative clues. Rashkis and Welsh (1946) in fact list 12 signs obtainable with the Wechsler scale whose comparative presence or absence indicates the presence of anxiety in varying degree. These signs include, for example, indecisiveness, apprehension and compensatory psychomotor activity such as fidgeting. The significance of the quality of behaviour when sorting is discussed by Rapaport *et al.* (1945).

Interpretation of test results.—It is widely asserted (e.g. Eysenck, 1943; Diethelm and Jones, 1947) that the test failures of the neurotic are the consequence of his illness. The converse view is held by Babcock (1944, etc.) who asserts that the test results reflect genuine differences in patterns of endowment and in potential efficiency of functioning which predispose to the development of neuroses.

Alcoholism.—Halpern (1946) applied the Wechsler scale to compulsive

drinkers who had not drunk for two years, to alcoholics who were giving up drinking, and to chronic drinkers. There were no significant differences between the groups. The range and mean I.Q.'s were normal, and the verbal and performance I.Q.'s were about equal. None of the groups exhibited a characteristic psychometric pattern, but the subjects disliked tests involving numbers, the significance of which is not discussed. Teicher and Singer (1946), however, found a rather consistent Wechsler Bellevue pattern in 10 alcoholics as follows: $V > P$; Comp. slightly less than Voc.; $Inf. > Voc.$; $Arith. > Dig.$; Span; Sims. = Voc.; Pict. Arr. poor and $< Pict. Comp.$; Obj. Ass. worst of all; Block Des. best of the performance tests. Roe and Shakow (1944) compared with the 1916 Stanford-Binet test: (1) normals; (2) acute alcoholic psychotics; (3) chronic alcoholic psychotics; and (4) general paretics. There were no significant differences between the first two groups, but the acute cases showed tendencies in the direction of the chronics between whom and the normals the differences were significant. The chronic alcoholics failed in tests, such as Sentence Construction, Absurdities and Fables, which required ability to maintain a definite set, and also in tests of rote memory. The pattern of failures in the paretics was somewhat similar, but, on the whole, the alcoholics were generally superior.

Drug addiction.—According to Pescor (1944) both male and female drug addicts are persons whose school career and intelligence had originally been normal. Milton (1944) also found no deviation from normal on the Wechsler scale. Aldrich (1944a) reports that drug addicts are able to perform the Vigotski Sorting Test as well as normals of the same Wechsler level. An intensive study of two addicts when consuming and when not consuming morphia was made by Brown (1946). When consuming morphia, although there were striking changes in the emotional sphere, the changes in intellectual performance were remarkably few, consisting merely of some reduced efficiency in Code Learning and Tapping Speed. Marihuana addicts, tested by Aldrich (1944b) with the Seashore Musical test, believed, when under the influence of the drug, that they had done better than when taking the test not under the influence of the drug, though in fact their performance was the same on both occasions.

Vitamin B deficiency.—Guetzkow and Brozek (1946) report that volunteers, after 161 days' partial restriction of vitamin B intake, showed no deterioration in performance of two tests of general intelligence or on the Porteus Mazes. After a further complete deprivation for 23 days, there was slight deterioration in tests requiring speed, and a lowering of level of performance on learning tests, although the rate of learning was unchanged.

The effects of alcohol, drugs and vitamins administered therapeutically are considered in the section on Treatment.

Miscellaneous organic syndromes.—Di Nolfo (1947) describes a battery of eight tests capable of being administered in 45 minutes by means of which the presence of "neurologic syndromes" can be detected in psychiatric patients. Cole and associates (1947a and b) made a comparison between normal subjects and patients with cerebral disease, with cerebral abscess or tumour, and with epilepsy due to meningitic causes or intracranial but extracerebral tumour.

The percentage of subjects with pathological Hunt Minnesota scores was 39 for the normals, and 71, 61 and 57 for the patient groups respectively. Of the Wechsler Bellevue items, those most affected were Comprehension, Digit-Symbol and Picture Completion. Other tests showed that the tumour patients were especially poor in spelling, wherein epileptics did better than the other groups. The cerebral diseased patients were characteristically poor in motor speed. Allen (1948a) found little to distinguish the brain-diseases from brain-injured patients with the Wechsler scale. In both groups there were defects in organizing visually presented material demanding analysis and synthesis of data, in prolonged attention and concentration, in motor speed and in visual anticipation and planning. Amongst cases with diseases of the basal ganglia tested by Brenner *et al.* (1947) three of four patients with Wilson's Disease showed no intellectual impairment, the other being impaired especially on Kohs' Blocks. They also found impairment in a Huntington's Choreic, even though the patient had too much disturbance of movement to take performance tests. Garmany (1944) tested a patient of originally high intelligence who suffered from changes following meningoencephalitis. Vocabulary functions remained good, but impairment was evident in the performance of such tests as the Matrices, Kohs' Blocks and Shipley Abstractions. Nyssen and Wens (1948) discovered some intellectual deficit in most cases of Parkinsonism. According to French (1948) the removal of cerebellar tumours in childhood is not followed by intellectual loss.

As in other organic syndromes, the qualitative aspects of the test performance have revealed defects of the Goldstein type. The paper of Halstead and Settlage (1943) is particularly important in this respect because they found the usual kind of defects in patients who had "made good or in some instances unusually good" social adjustments after removal of parts of the brain. Sorting tests were used also by Rashkis (1947b) in a comparison of schizophrenics, arteriosclerotics and paretics. The arteriosclerotics and paretics were alike in that their performance was "unco-ordinated" (whereas the schizophrenics' was "co-ordinated"), indicating defect in intellectual potentiality. The former, however, in contrast to the paretics, retained some critical evaluation of their performance, indicating that "the factor of intellectual organization is essentially unimpaired."

Review.—An excellent review of papers up to 1941 on the psychometric changes in organic brain disease is given by Klebanoff (1945).

Frontal lobe syndromes are discussed in connection with leucotomy (*vide infra*).

V. THE PSYCHOSES AND NEUROSES: GENERAL CONSIDERATIONS.

Relation of initial intelligence to psychoses and neuroses.—It is always difficult to be sure whether a low I.Q. is due to low innate potentiality or to the effects of the illness. Even in the neuroses, emotional disturbances may be present at the time of testing, thus vitiating the result. Nevertheless, Eysenck (1943) found the intelligence of neurotics not different on the whole from that of normals. Dewan (1947), on the bases of the test

results of over 30,000 men passing through an American Services Induction Centre, showed that emotional stability, judged by the subsequent history of the men, increased with increased intelligence. Birren (1944) compared the I.Q., obtained during school age, of 38 persons who subsequently became psychotic with that of persons who did not become psychotic. He

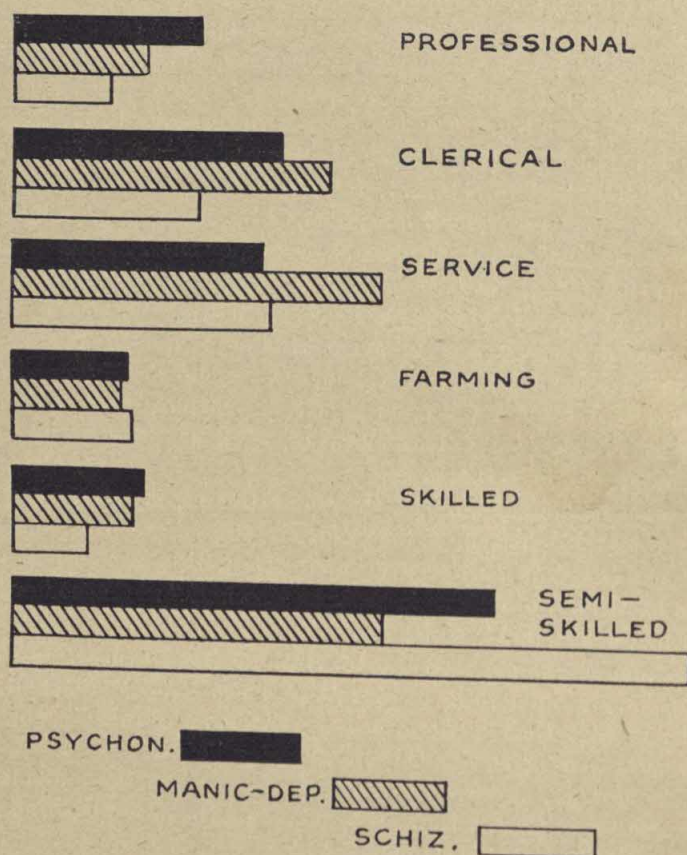


FIG. 1.—Distribution of psychiatric types in occupational classes (after Rabin, 1947).

found that children who subsequently developed what he calls "constitutional" psychoses had I.Q.'s significantly below the controls. I.Q.'s over 100 were found only among the future schizophrenics. A similar investigation by Wittman and Steinberg (1944) produced similar results. The range of I.Q.'s in the future schizophrenic was 63 to 123, but again, only the schizophrenic group included children of formerly superior intelligence. This method of following patients seems promising, but it must be remembered that psychotic tendencies which later become overt may be present in childhood, thus vitiating even school age I.Q.'s.

Rabin (1947*b*), who studied the vocational achievements in various conditions, states: "The patients show markedly lower representation in the occupations requiring higher intelligence, persistent effort and efficiency in competitive achievement," despite having reached normal educational levels. The distribution he found of psychiatric types in occupational classes is shown in Fig. 1. Rabin, however, carefully refrains from concluding that differences in vocational achievement reflect differences in native intelligence. He implies that in schizophrenia at least, native intelligence is normal and that the illness prevents the patient from achieving "early occupational adjustment commensurate with the individuals' capacities and educational background and opportunities."

Diagnostic Scatter patterns.—According to Penrose (1945*a* and *b*), a considerable percentage of psychiatrically abnormal persons, irrespective of the particular illness, can be distinguished from normals on the basis of the pattern of performance on a general intelligence test such as the Canadian Army "M" Examination. Perhaps the most interesting development in recent years has been the attempts to differentiate not merely abnormalities, but specific illnesses by means of Scatter patterns, particularly on the Wechsler Bellevue scale, which lends itself admirably for the purpose. These Scatter patterns are considered in more detail in later sections of this paper, but it should be stated at once that there is considerable disagreement among various authors about the constitution of these patterns. Others altogether deny the existence of specific patterns. Gilliland *et al.* (1943), for example, could establish no specific patterns on the Wechsler Scale for schizophrenics, paretics, manics, psychoneurotics, drug addicts, alcoholics or mental defectives. Where decline occurred it was global. Hunt and Older (1944) indicate that factors other than psychiatric disorder (e.g. cultural influences) may distort the psychometric pattern, and they conclude that Scatter can at the best only be suggestive. It must be remembered that deterioration indices are based on Scatter patterns and the unreliability and non-specificity of these has already been demonstrated. The quality of errors, as distinct from differential test ability, may be no more characteristic of different diagnostic groups, as was found by Lowi and Cohen (1945) in a study of comprehension of sentences exhibited tachistoscopically. No author claims more than about 80 per cent. agreement between psychometric and psychiatric diagnosis, and it is repeatedly evident that it is just in those cases where the clinical diagnosis is doubtful that the psychometric diagnosis is also dubious. There is even room for difference of opinion as to how well psychometric and clinical diagnosis agree in the individual case, as is illustrated by the contradictory views on the same material by Patterson (1946*a*) and Garfield (1947).

Although Rabin (1944*a*) has shown that amongst schizophrenics, test-retest consistency is fairly good, this does not prove that one group of schizophrenics is comparable with another, and, as Garfield (1948) shows, it is likely that disagreement between various authors is at least partially accounted for by differences in the types and severity of the illness from which similarly labelled groups suffered. In this connection Welch and Long (1946) found that abstract reasoning was disturbed more according to the severity of illness

than diagnosis. Another factor which various investigators have failed to keep constant is age. In fact, Foster (1947) demonstrates in one case that the Wechsler pattern of his patient fits the pattern described for his diagnostic group by Rapaport only if the raw scores are considered, and that if the scores are adjusted for age according to Wechsler's tables, the diagnostic pattern disappears. Thompson, (1946) demonstrated the same point in regard to others of Rapaport's supposedly diagnostic patterns.

It is thus clear that diagnosis by means of psychometric pattern is still uncertain and that the following sections on Schizophrenia, Manic-depressive Psychosis, Psychoneurosis and Epilepsy must be read with the above general considerations in mind.

VI. SCHIZOPHRENIA.

Wechsler Bellevue scale.—According to Wechsler (1944) the characteristic schizophrenic pattern on his scale is Verb.>Perf.; (Pict. Arr. + Comp.)<(Inf. + Block Des.); Obj. Ass. much <Block Des.; very low Sims. with high Vocab. and Inf., the last feature being pathognomonic. The inter-test variability is great, and greater in the Verbal than Performance tests. A most exhaustive study has been made by Rapaport and his colleagues (1945). This has been hailed as a masterpiece in many quarters, but with Alexander *et al.* (1947) we question the value of conclusions which have to be so often qualified by such phrases as "some impairment," "relatively efficient to a lesser extent," etc. The mass of statistics, tables and graphs is impressive, but as Line (1948) argues, does not clarify any current problem. The main conclusions of Rapaport's book seem to be that schizophrenics as a whole are distinguished from depressives by the absence of gross failure on every one of the performance tests; schizophrenic deterioration is characterized by extreme lowering of verbal test level below vocabulary level; Information and Block Design tend to remain high, but all groups except the paranoids are lower in Comprehension than Vocabulary; Picture Arrangement and Picture Completion are impaired in all schizophrenic groups. Olch (1948) discovered no significant difference in I.Q. between schizophrenics and normals, but younger schizophrenics were inferior on Dig.-Symb., Comp., Sims., and Pict. Comp., older schizophrenics failing in addition on Pict. Arr. Weider (1943) found that the Dig. Symb. item best distinguished young schizophrenics from normals, but that older patients were also inferior to normals on Obj. Ass. and Pict. Arr. On retesting schizophrenics one to thirty-five months after an initial test, Rabin (1944c) found the Verbal items more stable than the Performance. Comprehension fluctuated most and "seemed to offer to the patient the greatest opportunity of demonstrating thought disturbance."

Although Magaret and Wright (1943) discovered some differences between the Wechsler patterns of schizophrenics and morons, they stress not only the unreliability of most of Wechsler's signs for schizophrenia, but also the uncertainty of *any* diagnosis based on psychometric pattern. Garfield (1948) noted very great individual differences amongst schizophrenic subjects, and, like Gilliland *et al.* (1943) he also concluded that there is no pattern specific

to the condition. Brecher (1946) indeed showed that the application of Wechsler's signs would lead to a correct diagnosis in only 32.5 per cent. of cases and to a wrong diagnosis in the remaining 67.5 per cent.

Terman-Merrill test.—Myers and Gifford (1943) claim that a pattern which distinguishes schizophrenics from normals, neurotics and recovered schizophrenics, can be obtained with the Terman-Merrill test. Compared with other items of the same age level, items easiest for the schizophrenics are Vocabulary, Abstract Words, Memory for Sentences, and Digit Repetition, while hard items are Verbal and Picture Absurdities, and Memory for Designs and Stories. Font (1943), who illustrates a similar use of this test, states that the Terman-Merrill pattern reveals defects similar to those on the Wechsler scale and Shipley-Hartford test.

Babcock test.—The schizophrenic pattern on the Babcock test has been studied by Rapaport and his colleague (Schafer, 1944; Rapaport, 1945). Schizophrenics can be distinguished from depressives by their relatively good motor performance, and from neurotics by their failure in delayed recall. The greater efficiency of schizophrenics in repetition of digits than in paragraph learning indicates greater preservation of passive than of active attention.

Miscellaneous tests.—Wittman's paper (1943) is especially important because of the attention paid to the co-operation of her subjects. She is impressed by the number of hebephrenics who were also classified as mental defectives, which she attributes to the absence in such persons, even in school days, of the drives and motivating interests necessary to make normal progress. Paranoid psychopaths were found to be superior to other patients on General Information, Orientation and Arithmetic, while schizophrenics, providing they are co-operative, surpass the others in Rote Memory, Ferguson Form Boards, and Vocabulary. Jastak and Stubbs (1947) find a marked difference in the performance by schizophrenics of two clusters of tests. Whereas the distribution of capacity scores and of verbal polarity scores is normal in all types of schizophrenia, orthotude scores were mainly below average (*vide supra* and Table III).

TABLE III.—*The Distribution of Capacity, Polarity and Orthotude Scores of 40 Patients with Dementia Praecox.*

Standard scores.	N.	Capacity. %.		Polarity.			Orthotude.	
				N.	%.		N.	%.
130 and above	3	7.5	.	1	2.5	.	0	0
110-129	8	20.0	.	11	27.5	.	1	2.5
90-109	17	42.5	.	16	40.0	.	4	10.0
70-89	10	25.0	.	9	22.5	.	11	27.5
50-69	2	5.0	.	3	7.5	.	10	25.0
49 and below	0	0.0	.	0	0.0	.	14	35.0

The authors state that "Orthotude may be clinically defined as the relevance of mental adjustments. It is the tendency of a person to do the right things at the right time, in the right place." According to Hunt and Older (1944)

schizophrenics score about equally on the Kent Oral, Verbal Opposites, Easy Directions and Arithmetical Reasoning, with a slight but insignificant superiority on the last two tests. Eysenck's (1945) schizophrenic subjects made scores little better than her demented patients (about M.A. 8) on a Board form of the Matrices test. Penrose (1945*b*) makes the interesting observation that the pattern of schizophrenics on the Canadian Army Examination "M." differs from that of manic-depressives in much the same way as the pattern of normal females differs from that of normal men.

Schizophrenic thinking.—The main interest in the application of tests to schizophrenics is naturally the insight given into the thought processes in this disorder. Nearly all authors emphasize the special qualities of schizophrenic mental test performance—the bizarreness, the illogicality, the use of purely personal frames of reference. A number of essays on these and other aspects of schizophrenic thought have been collected and edited by Kasanin (1944). Goldstein (1943*a*) claims that these types of disturbance also derive from disturbed categorical attitude. He believes that whereas the organically affected patient is ruled by the environmental situation, rigidity in the schizophrenic is due to the projection of personal ideas on to the environment. Cleveland and Dysinger (1944), however, showed that the degree of concreteness in a test performance somewhat depends on the test, for, as previously stated, some schizophrenics could produce verbal abstractions, although they could not sort objects on an abstract basis. Rashkis (1947*b*) reports that schizophrenics were able to solve his number and word sorting test "with little impairment of performance potentiality." Although they could offer explanations of their actions, these explanations were often unrelated to what they were actually doing. Rapaport *et al.* (1945) applied the Vigotski-Hanfmann-Kasanin sorting test to schizophrenics, most of whom lacked the high intelligence required for the results to be reliable. On other sorting tests the schizophrenic's groupings were characteristically loose. In contrast to all these reports, Welch and Diethelm (1948) state that failures in a test of inductive reasoning "occurred in schizophrenics with marked anxiety and never in those without anxiety, demonstrating that some of the thinking difficulties are related directly to anxiety."

Schizophrenic deterioration.—Shakow (1946) distinguishes "capacity," "capability," and "ability." "Capacity" is the optimum potentialities of an individual, only revealed in emergencies. "Capability" is the optimum level of day to day performance, "Ability" is the usual level of day to day performance. Shakow believes that deterioration in schizophrenia may affect any level. He finds, on the whole, that poor co-operation has a less adverse effect on mental test performance than the psychosis. Wittmann (1943), on the other hand, "corroborates the findings of previous psychological studies which have indicated that the so-called 'deterioration' in schizophrenia is due to attitudinal factors of indifference and apathy rather than to any true 'dementia'."

Schizophrenia in children.—The study of schizophrenic children should be particularly rewarding precisely because of the absence of complicating features, such as prolonged hospitalization. The Stanford-Binet, Wechsler, Drawing-a-

man, Rorschach and other tests were applied by Des Lauriers and Halpern (1947) to over 100 schizophrenic children. In the intelligence tests, unevenness was the outstanding characteristic, breaks in success being often the result of preoccupation with some irrelevant detail of the data. In the drawing there occurred bizarre distortions, especially over-emphasis of extremities and confusion about the body's relation to space and the environment. This last finding recalls Bleuler's demonstration of the same point, and suggests that a topological approach to this matter may be fruitful.

VII. MANIC-DEPRESSIVE PSYCHOSIS.

According to Rapaport and his colleagues (1945) depression produces impaired motor activity which results in poor scores on the motor tests of the Babcock test and a generalized defect on *all* the performance items of the Wechsler scale. Defective performance of *all* the non-verbal items of the Wechsler scale is pathognomonic of depression whether of the manic-depressive or anxiety type. Ideo-motor retardation probably also accounts for the pathological scores on the Hunt-Minnesota test made by Meehl and Jeffery's melancholics (1946). Eysenck's manic-depressive subjects (1945), like her schizophrenics, made Matrices scores a little higher than demented patients. The correspondence found by Penrose (1945*b*) between the Schizophrenia-Manic-depressive axis and Femininity-Masculinity has been mentioned.

VIII. PSYCHONEUROSES.

Intelligence level of psychoneurotics.—Eysenck (1943), on the basis of the Matrices scores of 3,000 admissions to a neurosis hospital, concluded that neurotics do not, on the whole, display lower than normal intellectual potentialities. The distribution of scores was a little abnormal in that more than expected numbers clustered on either side of the mean. Amongst a smaller group of neurotics closely investigated by Ruesch *et al.* (1946), Wechsler Bellevue scores were normal. Halstead (1943*a*), on the other hand, found that 700 service neurotics scored, on the whole, below normal on the Matrices test and Shipley-Hartford vocabulary test, although unevenness of performance, so often said to characterize neurotic test performance, was not prominent. Similar inferior performance, but with wide dispersion of scores, on a Cattell test, was reported by Halstead and Chase (1944). Amongst 2,500 "psychosomatic casualties" tested by Torrie (1944) with the Matrices test, 44 per cent. scored below and 6 per cent. above average.

With regard to the different varieties of psychoneurosis, Eysenck found that conversion hysterics tended to be inferior, and patients with chronic anxiety superior to the others. Male psychopaths had high scores, whereas female psychopaths had low scores, which, Eysenck argues, reflects the fact that where there is no suspicion of poor intelligence, psychopathy is more often diagnosed in men than in women. Amongst 4,500 consecutively admitted prisoners tested by Gurvitz (1947), 851 were psychopaths whose intelligence distribution was the same as for the non-psychopaths. His tests included Digit-Symbol, Recognition, Paper Form-Board, Non-verbal Analogies and

Counting. Slater (1945), using the Matrices, Cattell and Shipley Vocabulary tests, found that obsessionals have a higher general level than anxiety, hysteric and other "miscellaneous" neurotics, amongst whom scores were about equal. Superiority of obsessionals over other neurotics was also observed by Rapaport *et al.* (1945).

Wechsler scale pattern.—Wechsler (1943, 1944) states that whereas in neurotics V.>P. in young psychopaths, P.>V. Also in neurotics (Pict. Comp. + Block Des.) is "generally" greater than (Pict. Arr. + Obj. Ass.), while in the young psychopath, the latter sum "nearly always" exceeds the former. Both groups are distinguished from psychotics by less inter-test variability, even though inter-test variability is greater in neurotics than in normals. Rapaport *et al.* (1945) stress the importance of the presence or absence of depression as a factor in influencing the pattern, for, as already stated, its presence, *pari passu* with its severity, impairs performance on all the non-verbal items. He distinguishes among the neurotic subgroups, neurasthenics by their poor general level, obsessionals by their high general level, anxious, hysterical and "mixed" neurotics by higher scores on Similarities than on Vocabulary. Lewinski (1945*a*), however, found no consistent psychometric pattern amongst 25 anxiety neurotics, not even Verb.>Perf.

Pattern on Babcock and Matrices tests.—Rapaport and his colleagues (1945) report that depression, when present, leads to defects on the motor tests. Neurotics were chiefly distinguished from schizophrenics by good learning in the delayed recall item. According to Himmelweit (1945) a high Matrices—low Vocabulary pattern occurs in hysteria, the reverse picture in anxious or depressed neurosis. She hazards the suggestion that these two patterns may be associated with extra- and introversion.

Abstraction tests.—Amongst others, Rapaport *et al.* (1945) and Welch and Diethelm (1948) applied sorting or similar tests. The former found that neurotics performed fairly well, although obsessionals were characteristically narrow in their grouping. The latter, whose subjects were children and adults with various types of mental illness, made the important observation that, whatever the diagnostic group, failure occurred only when anxiety was present. Improved or normal results were obtained on retesting eighteen patients after anxiety had subsided.

Miscellaneous.—In an interesting paper, Lewinski (1945*b*) reported a correlation of .536 between the rank order of difficulty of the Wechsler scale items for migrainous and normal subjects. This correlation is larger than that between neurotics and normals, but smaller than that between neurotic and migrainous patients. Elsewhere (1947), he reports $\rho = .936$ between patterns in migraine and epilepsy. The migrainous subjects performed best on Object Assembly, Block Designs, Picture Completion and Comprehension, and worst on Digits, Picture Arrangement, Information and Arithmetic. Carbon (1946) found that the Stanford-Binet responses of child stammerers indicate that while they succeed on verbal items, they are "markedly inferior" in handling non-verbal material. Keir (1945) tested a girl both in her normal state and under hypnosis who, under hypnosis, assumed the personality of a school child. The failures and successes in both conditions corresponded

with the personality prevailing at the time. The Slaters (1947) were able to differentiate male homosexuals from normal men by their response to a Selective Vocabulary test.

IX. EPILEPSY.

The performance by non-institutionalized epileptics on the Canadian Army Examination "M." does not significantly deviate from normal (Sheps, 1947). Mayman and Rapaport (1947) review the literature with a view to ascertaining whether epilepsy causes impairment of intellectual functioning, and if so, why; and if there is a specific psychometric pattern in epilepsy. They conclude that there is as yet no certain answer to any of these questions. Deterioration occurs in some cases, but is *not* characteristic of convulsions in general, and may be due to some other factor. Of 85 epileptics to whom the Stanford-Binet test was applied by Falk *et al.* (1945) in 1935, 1938 and 1944, only 3 showed any evidence of deterioration and these were psychotic. The same test was used by Hilkevitch (1946) in a study of 66 Epileptics, 26 of whom were retested at intervals up to 11 years. Her conclusion also was that deterioration was infrequent, and that when it occurs, it is noticeable soon after the onset of the disorder and is related to the frequency of fits. She believes that "one may be dealing with feeble-mindedness concomitant with epilepsy rather than the result of it." In an unpublished investigation of 292 epileptics with the Terman-Merrill, Wechsler, and Kuhlman scales, Reed, too, found a high association of epilepsy with mental deficiency, and believes that, where present, "this association is probably present from birth." Reed doubts "if deterioration of epileptics is as widespread as is commonly believed. Excessive scatter does not appear to be characteristic of epileptics except those having high mental ages. Whether or not there are certain mental functions in which an epileptic is superior or inferior is still an open question." Johnson (1947) calculated Wechsler's Deterioration Quotient in non-epileptic morons and in two groups of epileptics, one with I.Q. above, the other with I.Q. below 80. The correlation between C.A. and D.Q. was highest in the epileptics with I.Q. above 80, lowest in the non-epileptic morons, which seems to indicate that intellectual deterioration occurs more frequently in the more intelligent epileptics. An alternative, and more likely explanation, is that where the I.Q. is low there is from the beginning such poor performance of the "Don't Hold" items, that the passing of time cannot decrease it further. The correlation between D.Q. and duration of seizures was lower in the more intelligent group.

An excellent paper on epileptic and non-epileptic twins was published by Lennox and Collins (1945). Comparison of the epileptic with the non-epileptic partners of monozygotic twins showed that the former were inferior only where there had been brain injury, from which it is concluded that, granted good original endowment, epilepsy does not produce deterioration in the absence of brain injury. Amongst dizygotic twins, however, chronicity was associated with inferior performance.

The Wechsler pattern in epilepsy has been compared by Lewinski (1947) with that in migraine ($\rho = .936$), in neurosis ($\rho = .718$) and in normality ($\rho = .33$). Even granting that migraine may be related to epilepsy, the

high correlation between the patterns in epilepsy and neurosis is said to support those authors who have explained much of the epileptic's behaviour as neurotic reaction to the disorder rather than as the result of the illness itself. Lisansky (1948) found greater similarity than difference between the performances of diabetics and epileptics on the Wechsler scale and Rorschach. "The weight of evidence," she states, "is against the existence of a typical and fixed epileptic personality which characterizes all or even most epileptic patients."

It must be pointed out that none of the above investigations disprove the possible existence of a psychometric or personality pattern which, though it may occur in only a small proportion of epileptics, is found in no other variety of patient.

Twitchell-Allen (1947) reports the fascinating case of a man, aged 23, who, after 17 years of seizures, appeared to be "completely deteriorated." Substitution of phenytoin sodium for phenobarbitone controlled the fits. Then the patient was submitted for $4\frac{1}{2}$ years to intensive re-education and re-ablement. His M.A. improved from 6-7 to 13-2. He was finally able to hold a job, earn wage increases, swim, play the piano, and buy war bonds.

X. TREATMENT.

Psychotherapy.—Harris and Christiansen (1946) discovered no significant differences in the Wechsler I.Q. between groups of psychosomatic patients whose response to psychotherapy was good, fair and poor. The average I.Q. of the combined groups was 108.

Hormones and vitamins.—Both hormones and vitamins were administered by Vernon and McKinley (1946) to senile patients. Tests before and after treatment revealed no improvement in either intellectual or psychomotor performance, but, as the authors take care to mention, these subjects were receiving a full diet and consequently did not exhibit defects which in others may be improved by such treatment. A 19-year-old girl of Mortell's (1946) suffering from idiopathic hypoparathyroidism with mental deterioration, failed to improve her score on the Terman-Merrill, Wechsler and other tests, after treatment, which nevertheless produced physical improvement.

Glutamic acid.—Zimmerman *et al.* (1946, 1947) have reported astounding improvements in mental defectives following glutamic acid therapy. The most striking improvement occurs in the most retarded subjects and is displayed more in mainly verbal scales such as the Stanford-Binet than in tests involving motor skill such as the Arthur Point Scale. The rate of gain in M.A. slows down after six months' medication, although it remains higher than expected from natural increase in C.A. (Zimmerman *et al.*, 1948). Emotional stability also increases, and, indeed, Albert and Waelsch (1946) believe that the increase in test performance is more probably due to increased attentiveness, persistence, and emotional stability than to increased intellectual power, a view substantially that also of Jastak and Stubbs (1947).

Hyoscine.—An encephalitic patient of Cofer's (1947) showed some over-all improvement on all the subtests of the Wechsler scale, except Information, Digits and Object Assembly, while taking hyoscine with relapse when treat-

ment was suspended. Here, too, the author is inclined to look for the explanation of the improvement in the emotional field and in liberation of energy.

Sedatives and euphorants.—According to Sargant *et al.* (1945) small doses of alcohol or of sodium amytal, such as might be given to allay air-raid fright produce no decrease of ability on the Matrices test. Similar results were obtained by Arkola (1947) on the Hunt-Minnesota test after doses of $1\frac{1}{2}$ gr. of sodium amytal. Thirty-eight out of 50 neurotics tested by Damrau (1946) with a group test of intelligence improved their score after bromide sedation owing to relief of nervousness and tension. Phenobarbitone $\frac{3}{4}$ gr. was not so effective. University students investigated by the Kleemeiers (1947) increased their scores after ingestion of 10 mgm. of amphetamine, on a number of timed tests, owing, the authors suggest, to increased flexibility. There was no differential effect on fast and slow workers. Synhexyl, studied by Stockings (1947), produced little or no deleterious effects in therapeutic doses on the intellectual performance of normal controls. In seven melancholics, however, to whom selected Terman-Merrill items were given, memory functions involving reasoning power and logical interpretation were slightly affected, though more mechanical memory was unchanged. Pond (1948), some of whose tests were psychophysical rather than psychological (e.g. holding breath), maintains that synhexyl impairs rather than improves performance.

Electrotherapy.—Stone (1947a) administered the Wechsler memory scale to 15 patients before and immediately after a course of E.C.T. There was a mean loss of 17.1 points, amounting to 15.1 per cent. of the initial score. A second group of 14 patients, tested one day before the last treatment and two weeks later, showed a mean gain of 23.1 points, which constituted 27.9 per cent. of the first score. A further group of 15 patients (Stone, 1947b) was repeatedly tested with 5 separate forms of the Army Alpha, one day after the 1st, 9th or 10th, 19th or 20th and last treatments, and finally about three weeks after the last treatment. There was a decline during treatment, followed by a rise afterwards. In some cases, available high school and college entrance test results supported the view that the pre-illness level may be regained within a few weeks after E.C.T. although "sometimes lingering symptoms of illness may mask the progress of recovery of cognitive function." "Scores from the Wechsler memory scales are highly correlated with scores from the Army Alpha tests of intelligence given at corresponding times. In view of this and other evidence, it is suggested that in appraisals of electro-convulsive shock we are concerned with a generalized alteration of cognitive functions of which memory changes are only an integral part."

Luborsky (1948) tested 5 schizophrenic and 5 depressed patients before treatment, after the 10th or 11th E.C.T. and five or six days after "a complete course" of 12 shocks. During treatment the psychometric pattern of the schizophrenics resembled that in organic dementia. Impairment occurred in Block Design, Digit-Symbol, Word Memory and Picture Description tests. Vocabulary was affected least. In both groups impairment had disappeared at the last test. The reason, according to the author, for changes occurring largely in the schizophrenics is that the pre-treatment tests were more valid in those patients than in the depressives. Amongst the patients of Heuyer

and Peras (1943), tested on Digits Forward and Reversed, Designs from Memory, and Paragraph and Sentence Memory, only one, a boy of 14, showed decline of performance immediately following a course of E.C.T. Follow-ups were not reported.

Huston and Strother (1948) applied the Babcock and Shipley tests to 64 manic depressive patients, of whom 44 were depressed, 3 circular and 5 hypomanic; to 22 involutional melancholics and to 2 neurotic depressives. The average number of shocks was 7.8. The tests were given before treatment, 3 to 30 days after treatment, and 36 to 570, (average 189 days), later still. Vocabulary remained constant at about M.A. 17.0. The pre-shock scores were otherwise poor, reflecting the severity of the illness, and there was only little improvement soon after treatment, possibly because of confusion or residual symptoms. At the later follow-up, however, the scores were proved to be normal by comparison with a normal group matched for age with the patients.

Kogan (1946) reports an interesting case of a patient with meningo-vascular syphilis. Following antisypilitic treatment, a course of E.C.T. was given. His Wechsler pattern became less variable, but otherwise there was no change. Perlson (1945) records a patient who had received 248 shocks. At the age of 12 years 10 months and 14 years 6 months he had had I.Q.'s respectively of 130 and 116. At 29, after the treatments, he scored up to the expected level on six different tests, failing only a *timed* test of spatial orientation. "No gross intellectual or emotional impairment was elicited."

Electronarcosis.—The effects of electronarcosis have been studied by Harris *et al.* (1948) with the Wechsler and other tests. "Sixteen cases were tested both before and after treatment. Twelve of these showed losses averaging 4.4 points and 4 showed gains averaging 7.3 points. These changes are within the range to be expected on immediate retesting without intervening therapy and the findings suggests that the treatment has little effect on intellectual functioning, provided, of course, that an adequate measure is obtained before exposure to therapy. The over-all average change is a loss of 1.5 I.Q. points. This difference is in the opposite direction from that expected on the basis of practice effects; however, all of the loss is accounted for by slightly lower scores on the timed tests. Since these tests involve the learning of novel material, the loss may represent only the temporary inefficiency which many of the patients complain about immediately after a course of treatment." There was no consistent relationship between the amount of change and number of treatments or outcome.

Metrazol and insulin therapy.—Schnak *et al.* (1945) compared the performance of the Stanford-Binet, Kent-Rosanoff, and an aspiration test of 50 untreated schizophrenics and 50 schizophrenics treated with insulin or metrazol or both. Both groups improved their score between the pre- and post-treatment tests, but the gain was greater in the treated, especially metrazol treated, patients. On analysing the pre-treatment results, the authors were able to list various psychometric signs of a favourable prognosis. Amongst the good prognostic signs for insulin are M.A. > 15, Terman Vocabulary > 60 words; amongst those for metrazol are M.A. < 14, 5 or less Digit Reversed, and Basal Age 10 or less. The indications from the two lists, which contrast sharply, are that

insulin is likely to be more successful the better the personality integration, whereas metrazol is likely to be successful the greater the retardation. It seems, therefore, that electronarcosis is more akin to convulsive than to insulin therapy, for among the patients of Harris *et al.* (1948) those who responded well tended to be worse on timed than on untimed tests, a tendency not present in those who failed to respond.

Prefrontal leucotomy.—The number of papers containing psychometric data is remarkably small in comparison with the total number of papers on this topic. Freeman (e.g. Watts and Freeman, 1944) has repeatedly stressed the importance of life itself as a test of intellectual capacity and he quotes the very high achievements of many leucotomized patients to prove that intellect is not impaired by the operation. A difficulty arises from the fact that most leucotomized patients show pre-operative defects in psychometric performance. Kisker (1944), who applied Kohs', Weigl, Object Sorting and Rorschach tests, had only 2 patients among 20 who did not exhibit pre-operative impairment afterwards. Zeigler (1944) also discovered after operation no consistent or significant retrogressive change, except, perhaps, slight impairment of abstraction, which may have been due to a psychotic residuum rather than to leucotomy. Halstead *et al.* (1946) noted no evidence of a reliable or consistent shift attributable to leucotomy in Halstead's impairment index, a measure claimed to be especially sensitive to frontal lobe damage. Frank (1946) tested 96 patients with the Herring revision of the Stanford-Binet, a modified Terman-Merrill, Raven's Matrices, Kohs' and Passalong tests, but found no post-leucotomy abnormalities except in patients over 55 in whom the verbal test performance sometimes exceeded the non-verbal level by two or more M.A. years, a discrepancy which is in fact not abnormal at this age. Ström-Olsen *et al.* (1943) and Stevens and Mosovich (1947) also present essentially negative findings.

Some post-leucotomy defects have, however, been reported. In two extensive monographs Porteus (Porteus and Kepner, 1944; Porteus and Peters, 1947) has reported decline in his Maze test, noticeable particularly in the first six or seven weeks after operation; and, thereafter, a failure to improve with practice like normals. The quality of performance is also said to deteriorate. An interesting point is that the patients who subsequently most improved clinically showed the greatest initial decline in score and quality, but also the greatest subsequent improvement on the test. Porteus attributes the failures to loss of planning ability. Robinson (1946), too, discovered loss on the Mazes up to seven or eight months after operation. On tests of deliberation, speed of decision, volitional perseverance, and motor inhibition, leucotomized patients also fared worse than controls, because, she believes, of inability to sustain prolonged attention. Rylander (1947; Rylander and Sjöqvist, 1946) described after leucotomy, diminished speed in arithmetical problems, more concrete quality in interpreting fables and proverbs, and inability to name words in three minutes. A rather similar picture is drawn by Greenblatt *et al.* (1947) and by Malmö (1947).

The last investigations seem to us to be open to some criticism. In discussing intellectual impairment following leucotomy, one must, as always, distinguish between test-solving potentiality and test-solving performance-

between the weapon and its use. It seems to us that most of the reported defects affect the latter rather than former; and, granted the difficulty of making the distinction, it is nevertheless important from both the theoretical and practical aspects to avoid equating them. Robinson, in fact, states that leucotomized patients equalled the controls on Binet tests and in abstract thinking (Shipley Hartford), and actually exceeded them in learning (Hunt-Minnesota). Rylander acknowledges that the post-operative changes in the Binet as a whole and in many other tests were negligible. We consider the defect in word-naming hardly worth the emphasis he puts on it, as we find it a most unreliable test in adults, upset on the slightest and most varied provocation. Nevertheless, Rylander's patients were so carefully selected from the point of view of pre-operative suitability for testing that his results cannot be too lightly disregarded. Porteus's work is open to the further objection that most of the defects were observed in the first few post-operative weeks when the clinical condition is known to be transitory.

Babcock (1947) analysed the test performance of an anxiety neurotic before and after leucotomy. "He had changed from a well-concentrating person, able to keep a goal idea and to work persistently, to one of much weaker mental tension. He was slower in continuous work that depends on clear awareness. Perception was less reliable because of the over-quickness and mental confusion. It was as if his quicker functioning with the greater number of interfering associations kept his goal ideas from being as steadily effective. He doubled his time for the Turkish-English test, took the Memory for Story data as a record of a real event, was quicker but less accurate on Opposites, and had poorer Recall, Digits Reversed and Knox Cube scores. His speed increased but his accuracy decreased in the Word Recognition, Paired Associates and McQuarrie items." Even this well documented case is not, however, above criticism. The pre-operative Babcock index was 4.4, which, for a man of 27, is so low that one must suspect him of suffering from more than anxiety neurosis. The description of the patient also suggests the presence of manic-depressive elements, so that the post-operative performance, when the index had fallen to — 5.5, may have been adversely affected by mania, possibly released by the operation rather than by the leucotomy itself.

It is hardly surprising that the effects of prefrontal leucotomy are so variously reported since there is still no agreement about the effects of lobectomy, in which there is at least no doubt as to where the surgeon has cut. Goldstein (1944) reiterates his belief that signs of categorical impairment may be found in all cases of damage to the brain, especially to the frontal lobes, and including leucotomy, provided the patient is set tasks and situations of the right type to elicit the defects. Reports by others of Goldstein-type disorders after leucotomy and in other organic syndromes have already been mentioned. Using exactly the same methods as in his study of patients with frontal lobectomies, Rylander (1943) failed to elicit similar signs in patients with excision of tissue from other lobes. Halstead (1947) also concludes that certain impairments of function specifically follow frontal lobe damage. His book, which collects together his previously published papers on the effects on mental functioning under various conditions of organic stress or damage,

elaborate a concept of biological intelligence in which four new factors are statistically isolated. Yacorzynski and Davis (1945) also report poor grouping ability in lobectomized subjects. Their most interesting finding is the presence in these patients of perceptual disorders; for example, "the patients required a longer (tachistoscopic) exposure and greater illumination to perceive geometrical figures and words than the controls." They suggest "that symptoms which have often been ascribed as belonging to the fields of emotion and aphasia are due largely to the disturbed perceptual process."

On the other hand, Hebb (1945) in a provocative but important paper, insists that practically without exception, conclusions about the frontal lobe have been drawn from invalid material since the patients concerned had lesions or abnormalities other than in the frontal lobes. In the one case that he considers valid since the lesion was strictly localized to the frontal area, lobectomy produced no adverse change.

Section of the corpus callosum.—A series of eight patients on whom this operation was performed for relief of epilepsy was tested by Parsons (1943). "No picture of the syndrome of the corpus callosum" was reflected by the scores. A slight drop in Binet M.A. occurred in all except a boy of 14, but the drop was mainly in Digits Forward and Reversed, and Knox Cube. Vocabulary, Information, Reasoning and the Healy performance were mostly unaffected. Other aspects of these interesting patients are discussed by Smith (1945, 1947a and b, etc.) and Bridgman and Smith (1945).

XI. CONCLUSIONS.

We have attempted to mention the complete relevant literature published between 1943 and 1948 except in the section dealing purely with techniques. Completion in such a task is never accomplished and we apologize to authors and readers for the inevitable omission of material which has defied our search. We must now ask what is the value of this enormous output? Unfortunately, it must be admitted that it is largely negative. The limitations of certain procedures have been amply demonstrated, and this in itself is worth while, but on the positive side there is scarcely a single statement that has not been contradicted, and it is impossible to predict what the future will confirm. However, no mention has been made in these pages of the advances made in non-intellectual testing, and often when these are available, the intelligence test results become more significant. In a great many investigations such tests as the Rorschach, T.A.T. and M.M.P.I. were also given, with promising results. It must be recognized, too, that much of this work was undertaken to try to elucidate some of the problems of diagnosis and treatment about which psychiatric opinion is still divided, and since psychologists have hitherto had to work mainly on material as presented by psychiatrists, they were bound to reflect these divisions. For example, while the same patients may be diagnosed by different psychiatrists as manic-depressive, schizophrenic or schizo-affective, and rated as not moderately or severely deteriorated, what hope has the psychologist of eliciting psychological signs for a diagnostic group not in conflict with results from elsewhere? Indeed, where the psychiatric aspect is clear the psychologist, by means of techniques established long before the

period covered in this review, brings a precision not present in ordinary clinical work. The value of mental testing in mental deficiency, in the accurate assessment of condition and prognosis in uncomplicated organic dementia, in vocational guidance where this is important in individual cases, and in many other fields, must be recalled. It may be, however, that these very successes have hampered further progress, for they have fostered a type of investigation designed to render psychiatric concepts more precise, whereas these concepts are not always amenable to such refinement. The bold desire of Rapaport, Wells and others, to by-pass psychiatric concepts may therefore be justified, and in the future, collaboration between psychiatrists and psychologists should be arranged with this in mind.

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PERSONALITY TESTS: 1944-1949.

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SUMMARY.

GENERAL SUMMARY.

I. BACKGROUND OF RECENT ADVANCES IN PERSONALITY TESTING.

If the first World War may justly be said to have given a great impetus to the development and use of tests of intellectual ability, the second may be said to have done the same for tests of those less obvious, less clear-cut, and less easily measurable aspects of personality which lie outside the cognitive field. In both wars, new ideas developed through the pressure of urgent military needs were adumbrated in the years preceding in various small scale research studies carried out by isolated individuals; fused together in the crucible of war they have led to a very real advance in these difficult fields.

The first and most obvious problem calling for psychological investigation and the construction of suitable personality tests was presented by the very large number of soldiers, sailors and airmen who broke down under the stress to which they were exposed and who crowded the neurosis centres set up by the nations who took part in the war. It became not only desirable but imperative to screen out the potential neurotic, and many different methods were tried in an attempt to solve this problem (Eysenck, 1947a). It cannot be said that psychology was entirely unprepared to deal with it, because the same difficulty had arisen, although to a smaller degree, during the first World War; nevertheless, much concerted effort was needed before practical steps could be taken

to solve it and, even now, our knowledge in this field is by no means complete enough to make us consider the question a closed one.

The second problem giving rise to the creation and use of personality tests was that of officer selection. Again, this problem is not a new one, but, while in the first world war the contribution of psychology to its solution had been largely on the cognitive side, it was recognized very early in the second world war that other areas of personality contributed as much, or more, to the quality of the good officer or leader and that existing methods of assessing these areas were inadequate. Consequently, much work has been done on this vexed problem of officer quality (which includes, of course, selection of subjects for all sorts of special assignments, such as piloting an aeroplane, becoming a member of the Office of Strategic Services, and so forth). Appraisal of the results here must lead one to conclude that success, by and large, has been elusive, although we have gained much important systematic knowledge through work in this field.

The third great problem which has led to advance in the field of personality measurement has been the treatment of neurotic war casualties, either in Army Hospitals, or after separation from the Army, through such bodies as the Veterans' Administration in America. The Veterans' Administration has set up a huge training programme for clinical psychologists in America, an important part of which is devoted to research in this general field, and much has already been done by those connected with it to increase our knowledge and understanding of personality through a variety of testing procedures.

II. CLASSIFICATION OF PERSONALITY TESTS.

There are many different ways in which personality tests can be classified. Personality, in this context, may be defined as the integrated totality of character, temperament, intellect and physique. In this definition character is conceived as the more or less enduring and consistent pattern of a person's conation; temperament as his more or less enduring and consistent pattern of affection; intelligence as his more or less enduring and consistent pattern of cognition (MacKinnon, 1944). In talking about tests of personality, however, it is customary, though unjustified, to leave aside tests of intelligence and cognition generally and to concentrate on tests of an individual's orectic qualities. Intelligence tests have been discussed in another chapter, so we shall concentrate on tests of personality in this narrower sense.

In this field, a division has grown up during the war years, which is very widely accepted nowadays, dividing tests into "psychometric" and "projective." The former may be defined as implying a quantitative or mathematical measurement of a particular personality trait or function by means of well structured and objectively scorable tests; the latter concept was introduced by Frank in 1939, and was defined by him in that year as follows:

"A projective method for the study of personality involves the presentation of a stimulus situation designed or chosen because it will mean to the subject not what the experimenter has arbitrarily decided it will mean (as in most psychological experiments using standardized stimuli in order to be 'objective'), but rather whatever it must mean to the personality who gives it, or imposes upon it, his private, idiosyncratic meaning and organization"

It is difficult to accept this division as being of any scientific value. The terms "psychometric" and "projective" do not refer to opposing sides of the same dimension, but rather to a hotchpotch of different test dimensions and, indeed, it is often quite difficult to see which of these different dimensions a particular author is referring to in classifying a test as "projective" or "psychometric." The main dimensions along which tests may be classified are as follows :

(1) *Classification according to type of stimulus.*—Test material may vary according to the degree of *organization* or *structure* present in it. In highly structured material, the correct response is uniquely determined by the relations existing between the different parts of the test ; in less well-structured material, the discrimination of the parts, and their interpretation, often form the major task of the subject. This classification clearly does not imply a dichotomy ; there are different degrees of organization or structure from the typical intelligence test at the one extreme, through the relatively well-structured Thematic Apperception Test, the less well-structured M.A.P.S. or Rorschach Tests, to the almost entirely unstructured Stern Cloud-Pictures or the Buck H-T-P Test at the other. In general, we may say that the more firmly structured the test-material or the test-situation are, the more restricted will be the variety of ways in which the subject can react to the test.

(2) *Classification according to type of reaction.*—The two main ways in which the subject can react to the stimulus situation are the *verbal* and the *non-verbal*. These can themselves again be classified : the verbal mode of reaction into *written* and *spoken*, and the non-verbal into *autonomic* and *motor* response.

(3) *Classification according to method of response.*—The two main methods of response are the *creative* and the *selective*. In the creative type of response the subject is required to supply the solution to the problem quite unaided and entirely from within himself, while in the selective type of response he is merely asked to choose one of several predetermined solutions. While the selective response method is used more frequently in connection with intelligence tests, and the creative response method in connection with tests of temperament and character, this correlation is far from perfect, and interesting advances have been made recently by using selective responses in connection with such tests as the Rorschach, the Word Association, and the Sentence Completion.

(4) *Classification according to method of scoring.*—Scoring may be objective or subjective. Scoring is objective when only one symbol, numerical or otherwise, can be assigned to any particular reaction and when all observers would assign the same symbol to that reaction. Scoring is subjective when either there is considerable disagreement between different competent observers regarding the symbol to be assigned or when no attempt is made to assign a symbol at all, but only a general impressionistic interpretation is given of the subject's performance.

(5) *Classification according to interpretation of score.*—The final product of the subject's reaction to the stimulus, whether it be verbal or non-verbal, creative or selective, may be classified as being either *symbolic* or *non-symbolic*. Tests of fluency, of persistence, of suggestibility, of perseveration, or of level of aspiration give scores which are interpreted directly ; others, such as the

Frank Sexual Symbol Test, the Dream Interpretation technique, or most drawing, painting, and play tests and techniques make use of symbolic interpretation of the products. Both methods of interpretation may, of course, be continued in dealing with the results of any one test.

(8) *Classification according to mental mechanism used.*—Tests can be classified on the rather theoretical basis of the mental mechanisms believed to be employed in them. Thus, some tests are thought to call forth responses based on the principle of *projection* (such as the Character Interpretation Test, for instance); others are based on the hypothesis that responses are determined by the principle of *identification* (the Szondi Test); others still make use of *reaction-formation*, *regression*, and various other Freudian mechanisms. Clearly, little agreement can be expected on allocation of tests according to this principle, particularly as experimental evidence for the very existence of the mental mechanisms in question is almost completely lacking.

It is interesting to note in this connection that the one mental mechanism which "projective" tests do not usually employ, in the opinion of experts in this field, is the mechanism of *projection*. Sargent (1945), in her review of "projective" tests, makes a rather disingenuous defence of this confusing practice, as does Bell (1948) in his book on Projective Techniques. Semantic difficulties of this kind, however, have not prevented the widespread use of this term.*

The six principles of classification briefly discussed above are relatively independent of each other; all possible combinations of type of stimulus, type of reaction, method of response, method of scoring, interpretation of score, and mental mechanism hypothesized may be found. Frequently the same test may be used in different ways by different investigators, changing its classification under some of these headings.

In the discussion of individual tests which follows, we have laid the main stress on the test material, dividing our discussion into two parts dealing separately with structured and unstructured tests; it would not be advisable to subdivide our discussion further along the lines suggested because any one test would then have to be treated under different headings; the Rorschach, for instance, would have to be treated both under the headings of subjective and objective scoring, and so forth. We have preferred, for the sake of convenience, to discuss all data relating to a particular test in one place, but the various other distinctions mentioned should be borne in mind throughout this discussion.

* A word should be said here about the term "test." A test is defined by Warren (1934) as "a routine examination administered to individuals belonging to the same group in order to determine the relative position of a given individual in the group with respect to one or more mental traits, motor abilities, etc., or in order to compare one group with another in these characteristics." It will be seen that, if we accept this definition, a projection test becomes a contradiction in terms, as the "projective hypothesis" seems to deny the very existence of these mental traits which are presupposed in the definition of the term "test." By and large, then, it would appear that the term "projection test" has an unfortunate resemblance to the term "Holy Roman Empire," which was not, strictly speaking, an Empire, only intermittently Roman, and very far from holy; projection tests are not tests as the term is usually understood and they do not even claim to make use of the mechanism of projection as defined by Freud and his adherents. The term is a bad one and should be dropped from psychology.

III. STRUCTURED TESTS.

Verbal Tests. (Questionnaires, Inventories, etc.)

Personality inventories, which originated with the Woodworth Personal Data Sheet, during the time of the first world war, rely on the verbal report of the subject regarding a number of printed questions which are put to him, the answer usually being in the form "Yes" or "No"; sometimes a third alternative "?" or "Don't Know" is permitted. The questions differ very widely, both with respect to their subject matter and also with respect to the number included in any given inventory. The number of questionnaires in legion by now and the number of studies carried out using questionnaires is much too large to be adequately summarized in a chapter such as this. We shall discuss rather the main advances which have been made and deal with those tests which are most widely accepted nowadays. Summaries of work on questionnaires are given by Ellis (1946, 1947) and Ellis and Conrad (1948) with particular reference to their validity in both civilian and military practices. A detailed discussion of all tests available is given by Buros (1949) in his invaluable series of Mental Measurement Year Books, the third of which has just appeared.

There have been eight main developments in the construction and use of personality inventories. Not all of them are found in any one test and most of them were foreshadowed in earlier work. These developments are as follows:

In the first place, scales have ceased to be defined in terms of arbitrary interpretations; instead, meaning is attached to them in terms of operational definitions. If it is found that neurotics more frequently than normals answer the question "Have you had many headaches?" with "Yes," it is not assumed that neurotics in actual fact have more headaches; this may or may not be true. What is scored is simply the relative frequency of endorsement of the item regardless of the truth or falsity of the answer or the motives underlying it. This change in emphasis makes scale construction much less of a subjective procedure and makes objective interpretation possible. It also leads inevitably to the second great development; the use of item analysis in the selection of questions to include in a scale. While technical publications dealing with item analysis have done so mainly in connection with tests of intellectual abilities (Long and Sandiford, 1935) the same procedures are now being applied to tests of personality.

The third great advance is the tendency to get away from some all-embracing index of abnormality, which includes neurotic, psychotic, introverted and other different tendencies, in one overall score, and to lay the stress, instead, on multiphasic scales, i.e. scales for separate syndromes leading to profiles of personality. These syndromes may either be isolated along clinical lines, as in the Humm-Wadsworth or Minnesota Multiphasic Personality Inventory, or they may be arrived at by means of factor analysis, as, for instance, in the case of the Guilford studies (1936, 1939a, 1939b). This use of factor analysis in connection with the construction of questionnaires constitutes a fourth advance.

The fifth marked improvement in scale construction lies in the use of separate scales for the evaluation of the truthfulness and accuracy of the subject's response; scales which can be used to correct the original scores or

syndrome scores derived from them. Examples are the "No-count" on the Humm-Wadsworth (1943) and the "Lie-scale" on the M.M.P.I. (Hunt, 1948).

The sixth improvement consists in the introduction of scales acting as "suppressor variables." As an example of this type of scale, we may take the "K" scale (Meehl and Hathaway, 1946). For the construction of these "K" scales a number of abnormal cases with high "lie scores" are chosen; because of the high "lie score," these cases would make normal scores on most of the diagnostic scales. They are then compared with normal cases showing similar scores on the diagnostic scales, but, of course, having low "lie scores." This comparison shows a differentiation between the two groups on a number of items, and a "K" scale, based on these items, is constructed and used to correct the artificially low scores of abnormal subjects on certain M.M.P.I. component scales.

The seventh suggested improvement relates to the use of alternative choice symptoms, i.e. the subject is not asked to admit or deny the presence of a symptom, but is rather asked which of two symptoms is more characteristic of him, the theory being that if both symptoms are equally undesirable the subject will have no chance of letting his wish to appear "normal" influence his score. It is essential, of course, in this approach, that for each pair of symptoms one should be frequently occurring in a normal group, the other frequently occurring in the abnormal group which it is intended to screen.

The eighth improvement, less important, perhaps, than the others, relates, not to the construction of scales, but to their method of administration. Instead of being given the printed questions with a request to fill them in in pencil, questions are printed on separate cards and sorted into boxes under the appropriate heading. This improvement is of little importance for normal, intelligent subjects, but has many advantages with dull or disturbed clinic patients.

We shall now discuss briefly the main scales in use at present, regarding which new work has been published during the past five years.

1. *The Humm-Wadsworth Temperament Scale (1942).*

This scale consists of 318 questions, only 159 of which are actually scored. From the answers to these items a seven-point profile is constructed, based on trait gradings or components derived from Rosanoff's theory of personality (1920). These are: *Normal*—characterized by the integration of temperamental make-up; *Hysteroïd*—irresponsible towards the social community, ethically inferior and dominated by considerations of selfish personal advantage; *Manic*—usually cheerful, active, alert, with versatile interests; *Depressive*—sad, inactive, hopeless and sluggish of thought; *Autistic*—seclusive, with a narrow sphere of interests and given to inward contemplation; *Paranoid*—self-sufficient, certain of his position, suspicious, militant in defence of his ideas, and *Epileptoid*—ecstatic, meticulous, inspirational.

The method of scoring the test is highly involved and results in each individual being given a score on each of these seven main tendencies, showing him to possess this tendency to a very strong, strong, moderately strong, borderline,

moderately weak, weak, or very weak extent, each of these seven divisions being subdivided again into three degrees—upper, middle, and lower. In addition, a No-count is derived which emerges from an observation that individuals who answer the questions with a high number of "No" responses (i.e. who deny the possession of the great majority of the tendencies expressed in the scale) tend, consciously or unconsciously, to obscure their real temperament. On the other hand, individuals with a low number of "No" responses may exaggerate their temperamental characteristics. These tendencies are thought to be due, on the one hand, to defensiveness, and, on the other, to suggestibility to the question. Consequently, the number of "No" responses is used to derive a No-count score which, if moderately extreme, can be used to correct the other components for this defensive or suggestible tendency and which, if extreme, is used to throw out the whole inventory as filled in by this particular person as being probably invalid.

The No-count is probably a very useful aid, but since frequently as many as 30 per cent. of normal subjects may invalidate their test in this fashion, the test tends to give scores of only about two thirds of those to whom it is given. Recently, supplementary techniques have reduced the percentage of rejections, but the effect of these changes on the validity of the test is as yet unknown.

The test was standardized and validated on clinical populations, but its main use has been in the industrial field. Although the original papers by Humm and Wadsworth (1943), as summarized in their manual, show a high degree of selective efficiency, more recent work by Poole (1942), Dorcus (1944), and Super (1947*a*) have given very much less successful results, particularly in the Army Air Forces Selection Programme in the United States. The questionnaire has also been applied to the selection of teachers by Seagoe (1945*a*, 1945*b*, 1946). Bluett and Beales (1947) have shown that in some selected clinical cases the profile on the Humm-Wadsworth Test shows a certain amount of concordance with psychiatric assessment of the case, but the number of cases and the method of selection used fail to make this study very convincing.

For clinical use, at least, there is no doubt that this scale is less useful than the M.M.P.I., to be discussed next. In the industrial situation and for military selection it is more difficult to be certain and it is probable that it is in the industrial field that the Humm-Wadsworth has its major sphere of usefulness at present.

2. *The Minnesota Multiphasic Personality Inventory* (1943).

This inventory consists of 550 statements which the subject sorts into piles, indicating them as being true or false with respect to himself, a doubtful category (" ? ") being also provided. These questions cover a wide area, including general health, neurological features; motility; sensibility; cardio-respiratory, gastrointestinal, and genito-urinary symptoms; educational, occupational, marital, sexual, religious, political and social attitudes; depressive, manic, obsessive, compulsive, delusional, phobic, sadistic, masochistic and other trends; and also items to indicate whether the individual is trying to place himself in an improbably acceptable light. On the basis of the

performance of patients in the various psychiatric syndrome groups, scales have been constructed for personality components.*

Additional scores are provided on four scales—the question score, the lie score, the validity score and the K score (Hathaway and Meehl, 1947). The question score simply records the number of “?” answers—a high score is taken to mean that the true scores on the diagnostic categories will, in all probability, be further away from the average than they are; the lie score is made up from the answers to a number of questions which make the subject appear in a slightly unfavourable light—subjects claiming a favourable alternative in each case are presumed to have falsified their diagnostic scales also in the direction of greater favourableness; the validity scale consists of items which are infrequently answered in the score direction by either normal or abnormal subjects—high scores, with certain exceptions, indicate that great care is necessary in interpreting the record; the K scale acts as a suppressor variable and is claimed to sharpen the discriminatory power of the diagnostic scales.

Work on this scale during the past five years has been considerable and has mainly been concerned with the following points:

(1) *Validity*.—Many studies have been carried out in an attempt to show how closely scores on the various M.M.P.I. scales are linked with independent criteria. Meehl (1946) reports a “blind” diagnostic study into three major abnormal categories on 147 hospitalized cases. Approximately two-thirds of actual abnormals were identified as such; of these about two-thirds were placed in the appropriate category of the three employed. Burton (1947) in a study of 20 rapists, 34 sexual inverts, and 84 other delinquents found significant differences between inverts and others on the masculinity-femininity scale of the M.M.P.I. Benton and Proebst (1946) compare scores of 76 patients on the nine categories of the M.M.P.I. with psychiatrists’ ratings. Agreement was significant on paranoid schizophrenia and psychopathy; depression and hypochondriasis were found to yield many false positives. The other scales yielded no significant results. Hunt (1948) in a study of 141 cases found no significant agreement between M.M.P.I. scales and “blind” diagnoses. Gough (1946a) gave the inventory to 136 patients and 27 normals. Neurotics gave profiles with two unequal peaks, scores on the neurotic triad (hypochondriasis, depression, hysteria) being higher than the scores on the psychotic triad (schizophrenia, paranoia, psychasthenia). For psychotics, the two triads showed equal scores. Severity of the psychosis was not indicated by the scores. Schmidt (1945) investigated 98 normal, white, enlisted men of the Air Force and 121 maladjusted soldiers. The inventory distinguished significantly between normal soldiers and those diagnosed as constitutional psychopaths, mild or severe neurosis and psychoses, and also differentiated between major clinical groups. Abramson (1945a) studied the relationship of the personality profiles of a series of 28 officers over a period of one year or more, finding good agreement between performance and inventory responses. Morris (1947) gave the

* Only 351 items are used in the construction of these scales. Other scales are in the process of construction and validation, which will, presumably, make use of at least some of the remaining items. The component scales are: (a) hypochondriasis; (b) depression; (c) hysteria; (d) psychopathic deviate; (e) masculinity-femininity; (f) psychasthenia; (g) paranoia; (h) schizophrenia; (i) hypomania.

scale to 320 naval personnel, including neurotics and psychotics, and found that it differentiated borderline normals from serious pathological cases, but was of no aid in the differential diagnosis of these cases. Clinical studies by Leverenz (1943) on 700 neuropsychiatric patients; Hampton (1947) on 407 college girls; Modlin (1947) on 416 U.S. army enlisted personnel; and Harmon and Wiener (1945) in their work on vocational advisement, have given evidence of the clinical usefulness of this scale.

Brower (1947*a*) showed high correlations between personality scores and cardiovascular measures in a mirror drawing test on 48 students. Rashkis and Shaskan (1946) found reduction in scores in depression, hysteria, paranoia and psychasthenia as a result of group psychotherapy, and Harris and Christiansen (1946) found that the M.M.P.I., as well as the Rorschach, predicted response to treatment of 53 patients suffering from physical disease or injury from which convalescence was delayed.

(2) *Correlates of M.M.P.I. scores.*—A number of studies have been undertaken to show that scores on the M.M.P.I. differentiate between different groups or are correlated with certain tendencies. Monachesi (1948) reports differences between 101 delinquent and 85 non-delinquent girls. Verniaud (1946) reports score differences between saleswomen, industrial women, and clerical women. Houk and Robertson (1946) show similarity of profile for neurotics and patients suffering from hypoglycaemia. Brower (1947*b*) shows negative correlations between I.Q. and hypochondriasis, hysteria and psychopathic deviation scores for 48 undergraduates. Brozek and Erickson (1948) report on changes in M.M.P.I. scales in experimental semi-starvation, while Abramson (1945*b*) found no change due to the ingestion of alcohol. No correlation was found by O'Gorman and Kunckle (1947) in comparing 490 fighter pilots who had no major accidents and 258 fighter pilots charged with accidents involving pilot error.

Lough (1947) found no differences between women enrolled in school teacher, music, nursing or liberal arts courses and college. Kimber (1947*a*), however, showed that Bible Institute students tended to have a higher number of nervous symptoms. Similarly, Bier (1948) found a seminary group more deviant and less well adjusted than medical, law, dental and other college students. Hewitt (1943) found 37 men members of Alcoholic Anonymous, as well as other drinkers, to show high scores on the psychopathic deviate scale. Berdie (1946) showed that restriction of range of interest is correlated with poor M.M.P.I. scores on hypochondriasis, depression, psychasthenia and schizophrenia. Harris (1948) suggests that a very high depression score, unaccompanied by other high scores, except on the paranoia scale, gives a favourable prognosis for shock therapy. This result is probably merely a statistical artifact.

(3) *Scoring methods and technique.*—Gough (1947) studied the effect of malingering on M.M.P.I. scales and found it possible to discover resulting profiles through the use of the lie and K scales. A similar study is reported by Hunt (1948*b*). Wiener (1947) found in 200 Veterans no differences between the individual and the group form of the test. Shneidman (1946) discusses a short method of scoring the M.M.P.I., and Manson and Grayson (1946*a*) suggest

a key-sort method. Ferguson (1946), Burton and Bright (1945), Krise (1947) and Mullen (1948) all make suggestions for improvement and rapid scoring, while Hathaway (1947) presents a profile coding system, and Welsh (1948) an extension of M.M.P.I. profile scoring. Drake and Thiede (1948) present an introversion-extroversion scale for the M.M.P.I., showing significant differences on introversion between students participating in many or few social activities. The F score is discussed by Kazan and Sheinberg (1945), who find that it indicates the presence of significant and often severe psychiatric disease. Meehl (1948) discusses the possibility of finding an "N" (normal) controlling factor in the test which is rather closely related to the "K" score, which is conceived as a suppressor variable. This approach is discussed in detail by McKinley and others (1948), Hathaway (1947), Schmidt (1948) and in great detail by Meehl and Hathaway (1946). It appears established that the use of the K scale does result in improved validity of the various component scales.

A different approach to the problem of the subject who is trying to appear in a favourable or unfavourable light is made by Wiener (1948), who used subtle and obvious keys for the various parts of the Minnesota Multiphasic, the assumption being that conscious or unconscious falsification of responses would affect the obvious keys more than the subtle ones. This approach is a very interesting and promising one, which deserves to be followed up in greater detail.

There can be little doubt that from the clinical point of view the M.M.P.I. is by far the most useful, promising, and valuable inventory yet produced, and as it is constantly being improved, it is unlikely to be superseded in the near future as the most valuable clinical instrument in the field.

3. *The Shipley Personal Inventory.*

The Shipley Personal Inventory is a group test for the preliminary screening out of potential neurotics. Its items are based on dissimilarities between neurotic and normal military personnel and are in a forced-choice form to promote valid answering, as mentioned earlier in this section. It is described in papers by Shipley and Graham (1946), Shipley and others (1946), and Shipley, Gray and Newbert (1946). There are two forms: a long one consisting of 145 items and a short form consisting of 20 items. The reliability of both forms ranges from .66 to .91 and the test shows a low negative correlation with intelligence in the neighbourhood of $-.3$. In one study by Shipley and others (1946) of 538 normal and 263 neurotic sailors, it was found that with the cutting point at eight, 69 per cent. of the neurotics were identified correctly, and 4 per cent. of the normals misclassified as neurotic. Similar promising results were obtained by Shipley, Gray and Newbert (1946) in a test of 1,004 normal and 385 neurotic sailors, and another study of 508 normal and 188 neurotic sailors. Berry, Graham and Mote (1946) showed that the correlation between the long and the short form of the inventory was very high and Smith and Voss (1946) constructed a special scoring key for officers.

The approach presented by Shipley is an interesting and a promising one, although it is doubtful whether most subjects could not see through the rather obvious attempt which is made to get them to give themselves away; also,

it is not clear whether in military selection, at least, such disguise is necessary. In an investigation described by Eysenck (1947a), the Shipley was given to a group of 500 normal Air Force cadets, as well as the Maudsley Medical Inventory (which is an undisguised 40-item neuroticism inventory). The two scales were correlated with psychiatric ratings made independently and gave almost identical correlations of .7, showing that for this group, at least, the special form of the Shipley has no advantage over the more usual kind. However, there can be no doubt that this method of test construction lends itself to a variety of different uses; for instance, it might be possible to put together items dealing with symptoms of equal social undesirableness, but characteristic of different psychiatric syndromes, asking the subject in each case to pick out the one that applied most nearly to himself. In this way, it might be possible to construct multiphasic scales not subject to some of the limitations of existing ones.

4. *The Cornell Selectee and Service Indices.*

There are two Cornell Indices—the Cornell Service Index (Weider and others, 1945) and the Cornell Selectee Index (Mittelman and Brodman, 1946; Weider and Wechsler, 1946; Wolff, 1946, 1947a, 1947b; and Harris, 1946b).

The Selectee Index contains questions of the usual "Yes"—"No" answer type, applicable to men and women between the ages of 18 and 40. The Cornell Service Index contains additional items applicable only to men who have completed at least six weeks of military training. Item analysis procedures were used in selecting these questions.

The Indices present one innovation over the usual type. They contain a number of "stop" questions which are considered of such importance that their endorsement is sufficient for referral to a psychiatrist, regardless of the total score. Some of the "stop" questions are "Did you ever have a nervous breakdown?"; "Are you a sleep-walker?"; "Have you ever had a fit or a convulsion?"; and so forth. Results from the use of this test are reported by Warner and Gallico (1945), who studied 1,300 non-psychotic patients and found results to correlate closely with histories obtained by interview. Moore (1947) found with almost 2,000 controls and 206 neurotics that the Selectee Index showed considerable differentiating power with long service groups. Harris (1946a) reports favourable results on 2,000 Seabee recruits. Manson and Grayson (1946b) found the Selectee Index to discriminate between 100 chronic "sick-book riders" and 100 unselected soldiers. Weider and Wechsler (1946) reported reliabilities in the neighbourhood of .9 and high tetrachoric correlations between inventory and psychiatric interview on 1,000 cases. Weinstock and Watson (1946), however, report unfavourable results on 212 recruits who were also given a routine psychiatric examination. Dynes (1946) gave the Selectee Index to 2,000 Naval returnees of whom 500 were survivors of sunken ships; only 5 per cent. of the total group showed evidence of severe nervous symptoms. Brodman and others (1947) compared 611 white and negro enlisted men on the Service Index and found that N.C.O.'s for both white and negro groups were less frequently neurotic than privates, and that neurotic patients with haemorrhoids, hernia, acute appendicitis and primary

atypical pneumonia were hospitalized longer than those without personality disturbances suffering from the same disorders. Leavitt (1946) compared the Neuropsychiatric Screening Adjunct (N.S.A.) with the Selectee Index, finding the former superior. Weider and others (1946) suggest the use of the Index in industry, research and general medical treatment.

On the whole, it does not appear that this index is significantly superior to any other well standardized inventory; the usefulness of stop questions has not, in our opinion, been proved beyond a doubt, but it is quite possible that this method may have useful features which would be worth while incorporating into an ideal inventory. In our experience, however, these "stop" questions correlate so highly with total score that they add very little, if anything, to the ordinary methods of scoring.

5. *The Guilford-Martin Temperament Profile Chart.*

This test is based on three inventories—the Guilford-Martin Inventory of Factors G.A.M.I.N., Abridged Edition; the Guilford-Martin Personnel Inventory I and the Inventory of Factors S.T.R.D.C. These scales are the end result of a lengthy and careful factorial study of a very large number of different items and problems.

The Inventory of Factors G.A.M.I.N. measure the following five traits:

- G—great pressure for overt activity.
- A—ascendency in social situations, leadership.
- M—masculinity in attitudes and interests.
- I—lack of inferiority feelings, self-confidence.
- N—lack of nervousness and irritability.

Reliabilities for these scales are almost exactly .9. The original 270 items were reduced to 186 in 1945 without apparent reduction in reliability.

The Personnel Inventory I measures three traits of the paranoid syndrome. It was originally constructed for the purpose of sorting out discontented individuals likely to make trouble. The three traits which it measures are:

- O—objectivity as opposed to subjectivity.
- Ag—agreeableness as opposed to belligerence.
- Co—co-operativeness as opposed to fault-finding and over-criticalness.

One hundred and fifty items give reliabilities between .8 and .9 for these three scores.

The Inventory of Factors S.T.R.D.C. deals with:

- S—social introversion—shyness and withdrawal.
- T—thinking introversion—meditation, introspectiveness.
- R—rhythymia—carefree disposition, impulsiveness.
- D—depression—feeling of unworthiness and guilt.
- C—cycloid—mood fluctuation.

One hundred and seventy-five items for these five scores give reliabilities in the neighbourhood of .90.

Martin (1944), in a validation of the Personnel Inventory I concludes that companies having an enlightened industrial relations policy could screen as

many as 85 per cent. of those workers predisposed to maladjustment through use of this Inventory. Adams (1946) has used this scale with some success in the prediction of adjustment in marriage, and Thomson (1947) has used it in the selection of executives.

The G.A.M.I.N. Inventory and the S.T.R.D.C. one are based on a series of factor analyses carried out by Guilford and Guilford (1936, 1939a, 1939b), while Martin (1945) describes the construction of this Inventory, which has been used by Luborsky and Cattell (1947). These factorial studies have been reviewed and reanalyzed by Eysenck (1947b), who concludes that the failure of the authors to find more general factors (introversion, neuroticism, etc.) is due to the particular statistical method they have adopted, and gives experimental evidence to show that this method has probably led to an incorrect conclusion in this instance. A similar result follows from Lovell's (1943) factor analysis of the thirteen variables of the Guilford-Martin Temperament Profile Chart. Basing her results on 200 undergraduates she found four significant factors emerging from the intercorrelation of the 13 scores, two of which are fairly clearly identifiable with general neuroticism and introversion-extroversion.

Until further validation studies are at hand, one hesitates to subscribe to the claims made by Martin regarding an 85 per cent. reduction in the employment of workers liable to neurotic breakdown, but there can be no doubt that the application of factorial methods to the construction of inventories of this kind will, in time, lead to definite advances. At present it is difficult to be more positive than that.

Other tests in this field can be dismissed rather briefly as little worth-while work has been done with them.

6. Using the *Wonderlic Personnel Test*, Wright and Laing (1943) showed that subjects' scores correlated highly when the test was given in a 12-minute period and when it was given in a 24-minute period.

7. The *Thurstone Inventory* was used by Burgess and Wallin (1944) to show a slight but significant degree of homogamy in personality characteristics of 1,000 engaged couples.

8. The *Maslow Security-Insecurity Test* (1945) consisting of 75 questions divided into three groups of 25 each has been shown to correlate highly with the Thurstone Neurotic Inventory, the Bernreuter Neurotic Tendency Score, and the Allport Ascendancy-Submission Test. It was used by Maslow and Szilavyi-Kessler (1946) to show a U-shaped relationship of security feelings to length of breast-feeding, suggesting that maternal rejection or acceptance is a fundamental determinant of security. Ansbacher (1947) used the S.I. Test in support of Adler's theory that recall was expressive of basic attitudes rather than a function of repression, as Freud believed. He did this by showing a certain amount of congruence between the earliest recollections of a group of college students and their scores on the S.I. Test.

Goldman (1948) also investigated the problem of the influence of breast-feeding on character and showed a significant difference in "oral optimism" and "oral pessimism" (as measured by a set of inventories constructed by her and shown to have internal consistency, both by an item analysis and a factorial

study) between adults who had been weaned early and adults who had been weaned late. Those who were weaned in the first three months tended to be "oral pessimists"; those who were weaned after the fourth month tended to be "oral optimists." Bottle-fed children were neither optimistic nor pessimistic on the average. Ansbacher (1947) used the S.I. Test in support of Adler's theory that recall was expressive of basic attitudes rather than a function of repression, as Freud believed. He did this by showing a certain amount of congruence between the earliest recollections of a group of college students and their scores on the S.I. Test.

9. The *California Test of Personality* was used by Alexandra (1946) to show that "elected leaders" in girl scout troops were better adjusted than non-leaders. Pfieger (1947) showed that a poorly adjusted child on the California Test will have a greater number of problems, as shown by the scores on the Mooney Problem Check List. Kimber (1947*b*) showed that scores on the California Test of Personality could be falsified in the direction of making the subject appear better integrated and argued that this showed "insight" into the items of a Personality Test. Even so, correlations between the artificial and the natural method of taking the test were above .5 for both men and women.

10. Brown (1944) reports an experimental study of his *Personality Inventory* for children on 77 neurotic and 200 normal children between 8 and 15 years of age, giving good discrimination. He also gives reliabilities and carries out an item analysis on total scores and subscores. This test, in the reviewer's opinion, is probably the best for use with children.

11. Seibert (1945) gave the *Johnson Temperament Analysis* to 154 women students and considered, in a large number of cases, that the test rating of maladjustment was clinically verified in an individual conference with the psychologist.

12. The *Woodworth Personal Data Sheet* was applied to 800 inmates of the United States North-Eastern Penitentiary by Pescor (1945), 17 per cent. of whom were considered to have a psychoneurotic tendency or to be definitely psychoneurotic. This percentage is rather low and suggests doubt about the standards employed. It is claimed that in a subsequent observation the Inventory score was found correct in about 85 per cent. of the cases.

13. The *Bernreuter Personality Inventory* was factor-analyzed by Martin (1948). Following up Flanagan's earlier work (1936), Martin found that most of the variance of the test was accounted for in terms of two factors which are similar to Flanagan's. Schmidt and Billingslea (1945) in comparing 95 normal soldiers and 329 psychoneurotic or psychopathic soldiers found, by means of a profile analysis, that they could obtain an 80 per cent. effectiveness in differentiating deviates from normals without, however, being able to diagnose the type of maladjustment. Patterson (1946) used the Bernreuter on a group of about 100 married couples who were parents of a group of children who were studied in a longitudinal child survey. A certain amount of homogamy is indicated and it was found that neurotic mothers appear to show types or parent-child behaviour commonly considered less desirable, while confident and dominant mothers seem to manifest the more desirable behaviour. There appears very little relationship between parents' personality, as measured by

the Bernreuter, and the personality of the child, as measured by ratings on the *Brown Personality Inventory* and scores on the *Vineland Social Maturity Scale*.

14. The *Bell Adjustment Inventory* was used by Fischer (1944) and showed a correlation of .42 between emotional maladjustment and lack of achievement at college. Nimkoff and Wood (1948) studied the relationship between courtship behaviour and scores on the Bell Adjustment Inventory. They found little relation between emotional adjustment and the onset of frequent dating, but students who start "going steady" early and who change "steadies" frequently are likely to be emotionally maladjusted. Similarly, students who "go steady" against the wishes of their parents tend to be emotionally maladjusted. Rose (1946) studied the influence of the war on scores on the Bell Adjustment Inventory and found greater insecurity, increase in emotional excitability, greater lack of control, increase in depressive tendencies, and greater anxiety. Smith (1947) found a relationship between scores on the Bell Adjustment Inventory and participation in extra-curricular activities, proving that social adjustment is evidently accompanied by a tendency towards participation. Tuckman (1946) reports a fairly high correlation between the Bell Adjustment Inventory and a 5-point scale which he calls the Adjustment Questionnaire. He interprets his finding as showing that a good estimate of an individual's adjustment can frequently be got through asking a few direct questions.

15. The *Allport-Vernon Study of Values* has been used by Gray (1947) to show that Southern white college girls deviated in the same way from the normative group as did Negro girls in the South, interpreting this finding as indicating the general effect of the Southern environment.

Friedman (1946) has constructed a new *Values Questionnaire*, dealing with the three values of physical activity, theoretic-scientific, and aesthetic tendencies.

16. The *Maudsley Medical Questionnaire*, a 40-item neuroticism inventory, carefully constructed through a series of item analyses and validation experiments, has been found to correlate highly with psychiatric opinion within neurotic army populations (Eysenck, 1947b). Mention has already been made of the fact that in a normal group of 500 cases the correlation between this questionnaire and psychiatric opinion of .7 was found (Eysenck, 1947a).

Others.

A number of interesting tests have been constructed following the principle of the *Pressey-X-O Test*. Thus, Bennett (1945) and Slater (1945) show significant differences between normal and neurotic soldiers using a method of analysis by means of discriminant function. Martin (1945a) reports on his *Worry Inventory*, and Wallen (1945, 1948) and Gough (1946b) showed food aversions to be significantly related to neurotic disorders.

An interesting approach to the problem of validity is presented by Zapf (1945a, 1945b), who constructed a *Superstition Test* of 100 items, results of which he found to be correlated negatively with intelligence, with emotional and social adjustment, and with socio-economic status. He also showed considerable agreement ($R = .79$) between results of the pencil and paper tests

and actual behaviour in situations calling for superstitious responses covered in the questionnaire.

Family relations were studied by means of questionnaires by Sherman (1946), who was interested in the emancipation of students from their parents, and by Essig and Morgan (1946), who found that daughters of employed women showed poorer adjustment than girls whose mothers did not work outside the house. Brown and others (1947) used their *Family Relations Questionnaire* to study the influence of affectionate family relationships on character development and showed that character development is related to sharing family decisions, parental attitudes towards the child's playmates, and interparental relations. Hohman (1947), Finger (1947) and Adams (1946) have worked on problems connected with sex life through questionnaires, the last named attempting to predict adjustment in marriage, a point also discussed in Terman and Oden's book (1948).

Closely related to all this work on personality inventories is the study of occupational interests. The main test there has been the *Strong Vocational Interest Blank* which has been exhaustively discussed in his book (1946). Its position has lately been challenged by the *Kuder Occupational Preference Record*, work on which has been summarized by Super (1947b). These two inventories admirably cover a part of the personality which the usual questionnaire does not pretend to deal with, and there is no doubt that from the point of view of vocational guidance and occupational selection they represent an important addition on the orectic side to the usual measurement of abilities and knowledge.

SUMMARY.

This short selection of some of the more important papers published in this subfield of personality testing will show that very much interest has been shown in questionnaire construction and validation. The main advances in the field have already been summarized, but we may, perhaps, briefly indicate what we consider to be the most important area of usefulness for questionnaires of this type.

It seems axiomatic that in the clinical situation no final verdict or diagnosis should ever be given on the results of an inventory alone; the same is true of counselling in the vocational guidance situation, and also in the field of "screening." In all these situations where the individual psychiatrist or psychologist is usually so overwhelmed with work that he cannot make an adequate appraisal of everyone, the inventory performs a useful role in indicating those most in need of help or most likely to be subject to breakdown.

The second function of the personality inventory is that it forms a kind of preliminary survey which, for any given patient, makes it possible for the psychiatrist or psychologist, in his interview, to locate and lay stress on certain areas which are likely to be important and to exclude others which are likely to reveal little of use to him.

In the third place, inventories, if properly used, can be of the utmost value in research, although it must be said quite candidly that a large percentage of the research carried out in this field is amateurish and relatively

worthless. This, however, should not blind one to the potential contribution that well constructed inventories properly used can make to the investigation of personality. It seems clear that a good deal of the dislike shown by experimental psychologists towards the very idea of inventories and questionnaires ultimately derives from the fact that many of these instruments are constructed and used by persons ignorant of the psychological and statistical principles involved, and having no worth-while scientific question in mind when carrying out their research. Similarly, in the practical field, the frequent lack of success in the use of inventories is often due to the failure of the individual worker to select the proper instrument and to use it to its best advantage. Like other fields of psychological testing, the use of inventories should be confined to the expert; too much damage has already been done by the amateur.

PERFORMANCE TESTS.

Of all the types of test discussed in this review, possibly the most important are those dealt with in this section. They come nearest to the ideal of objective empirical investigation; they suffer less from the evils of voluntary distortion, intuitive interpretation, or subjective recording. Our hope of building up a true science of personality rests on the development of this type of test more than on any other. No adequate summary is available in this field, but a historical survey of some of these tests is given by Eysenck (1947*b*) who has also attempted to link up results from non-verbal tests, on the one hand, with other types of both structured and non-structured testing technique, and, on the other hand, with psychiatric ratings and diagnoses.

1. *Suggestibility.*

While, in common parlance, suggestibility is regarded as a kind of unitary quality, Eysenck (1943*b*) and Eysenck and Furneaux (1945) have shown that there are at least two, and possibly more, different types of suggestibility quite uncorrelated with each other. The most important of these is called "primary" or "ideo-motor" suggestibility. This type of suggestibility consists essentially in the measurement of a person's reaction to a repeated suggestion that he should perform a certain kind of movement; in the *Body Sway* test, for instance, it is suggested to him that he is falling forward and his actual body sway, both forward and backward, is measured in inches, maximum sway either way constituting his score. This test has been shown to be highly correlated with a general lack of personality integration, or "neuroticism" (Eysenck, 1944), and also with hypnotizability (Eysenck, 1943*a*); the suggestible person tending to be easily hypnotized (Furneaux, 1946). No special connection was found between hysterical disorders and suggestibility; hysterics are no more and no less suggestible than other types of neurotic, contrary to widely held psychiatric opinion (Eysenck, 1943*b*). Sodium amytal injection was shown to increase suggestibility of neurotics who were already suggestible, but not to affect patients who were not suggestible to begin with (Eysenck and Rees, 1945). No tendency towards increased suggestibility has been found in epileptics, mental defectives, or psychotics (Brady, 1948; Eysenck, 1947*b*), so that this test appears to be a relatively specific measure of neuroticism.

Secondary suggestibility is connected with "gullibility" and is exemplified by tests in which the subject is led to believe that he will experience certain sensations (olfactory, gustatory, etc.) when, really, no such sensation occurs; his score is the number of times he is actually misled into accepting the existence of a non-existent sensation. This type of suggestibility is negatively correlated with intelligence, unlike primary suggestibility, which seems to be quite independent of the influence of cognitive factors. (It should be noted in this connection, however, that Curtis (1943) reports a correlation coefficient of .50 between hypnotic susceptibility and intelligence for 32 subjects. This finding is accountable in terms of a theory of suggestibility and hypnotic susceptibility given by Eysenck (1943a).)

Experiments in the field of suggestibility, other than the ideomotor type, include Luchins' (1945) demonstration of social influences on the perception of complex drawings; Kay's (1947) experimental study of prestige suggestion, which explores the influence of Frank Sinatra's campaign to change attitudes of adolescents, and Schonbar's (1947) study of the modification of judgments in a group situation. Also, mention might be made in this connection of Sherif's (1935) well known work on the autokinetic phenomenon which investigates the modifiability of subjective estimates due to group pressure. A factorial study of tests of suggestibility by Grimes (1948) largely supports Eysenck's study of 1946.

2. *Static Ataxia.*

It has been shown that simple measurements of static ataxia correlate rather highly with body sway suggestibility and this test also shows high correlations with "neuroticism" (Eysenck, 1947). A number of studies have been reported on different ways of measuring this phenomenon (Fisher and others, 1945; Jongkees and Groen, 1947; Seashore, 1947), while studies by Edwards (1943, 1946, 1947), Birren (1945) and Travis (1945) attempt a more careful analysis of the phenomenon of static ataxia.

3. *Persistence.*

Persistence is tested mainly in relation to the tendency of an individual (a) to continue a fatiguing or painful motor task when he is at liberty to stop, or (b) to continue a boring and unrewarding ideational task although, again, he is at liberty to stop. Persistence, along either of these two lines, appears to be correlated quite highly with neuroticism and it would also seem that hysterics are significantly less persistent than other neurotic types of patients (Eysenck, 1947b). Tests of this type have been found to be highly reliable (Dunlap and others, 1947) and their relation to scholastic achievement has been studied by Roach (1943), Schofield (1943), and French (1948) with conflicting results. A scale for the measurement of this quality has been constructed by Rethlingshafer (1943) and the dependence of persistence on previous experience has been experimentally investigated by Grosslight and Child (1947). A large range of 28 motor persistence tests has been studied by Cureton and others (1945) and the results are given in great detail. As one would expect from the fact that persistence and suggestibility are both correlated with

neuroticism, they intercorrelate to a certain extent (in neurotic groups, at any rate) (Eysenck, 1947b).

4. *Autokinetic Phenomenon.*

The autokinetic phenomenon consists essentially of the subject's impression of movement of a stationary small spot of light seen by the observer in a dark room and recorded by him on a piece of paper. This movement results, of course, from the absence of a stable frame of reference and has been shown to be of considerable interest in the study of the formation of social norms by Sherif (1936). Voth (1947) has used this phenomenon as what he calls a "projective measure of personality structure." Studying 845 patients, he found the autokinetic movement assumed a considerable variety of different patterns. He found it to be very pronounced in schizophrenia, epilepsy, psychasthenia, neurasthenia and anxiety states. He found it to be either absent or much less extensive in the manic-depressive and involuntional psychoses and in conversion hysteria. From his report it would appear that a limited or medium amount of movement is considered to be most favourable prognostically. His work, as well as that of Sexton (1945), who found that patients with schizoid make-up reported much greater movement than more "extroverted" personalities, may be related to advances in the field of expressive movements, which will be discussed later on. Schonbar (1945) and Bovard (1948) have followed up Sherif's original work on the effect of social norms on this phenomenon. There seems to be little doubt that studies of this type bear a close relationship to suggestibility and it would seem desirable for suggestibility tests to be included in any study of the autokinetic phenomenon.

5. *Expressive Movements.*

The main advance in this field has been the work of Mira (1939, 1945), which has been discussed by Simon (1943). Mira's method of myokinetic psycho-diagnosis rests on the principle that "psychological space is not neutral; all the movements of the individual acquire a peculiar meaning according to the direction in which they are performed." These movements are analysed in terms of certain drawing tests in which the individual has to draw, blind-folded, a series of circles, a staircase pattern, and so forth. The main direction of his movements is taken to be a clue to his personality. Mira (1940) has published certain data supporting this view, which fits in well with the much more extensive earlier work of Allport and Vernon (1933). A rather different approach is that adopted by Jones (1943a, 1943b), who observed the effect of mental arithmetic and of inhibition of micturition on the frequency and patterning of movements. His interesting work appears to be worth following up in the field of mental abnormality. Deutsch (1947) reports clinical studies of 17 patients whose postural behaviour is claimed to be expressive of their motivations, attitudes, intentions and reactions, both voluntary and involuntary, conscious and unconscious. This study is of the usual psychoanalytic type and gives little valid verification. Grace (1943) reports results from the use of a rating scale on the gait of over 100 women students from motion pictures, showing front, back and side-views of the usual manner of walking.

Interesting reports by Canestrelli (1941) and Filippini (1941) deal with the use of the photocyclographic method in which the movements of the subject's hand during rapid psychomotor work is studied by means of a photographic technique, and with the use of the pedomergograph, a study of the records of which is claimed to reveal fundamental personality traits. These studies of expressive movements tie in with work by Wenger (1948) and Ruesch and Finesinger (1943) on the measurement of muscular tension during handwriting. Duffy (1946) has also investigated the level of muscular tension as an aspect of personality and has shown that "tension level" is a more or less persistent characteristic of the individual, a conclusion based on a factorial analysis of "tension level" in the muscles of the hands on eight different tasks. Kennedy and Travis (1947), Loucks (1947) and Finch (1947) describe techniques of recording action potentials in muscle movement and, through them, different tension levels. Jacobsen (1943) has studied the effect of cigarette smoking on muscular tension with largely negative results. Other studies of interest in this field are those by Philip (1945) and Shipley and others (1945), who deal with problems of methodology. These lead over quite naturally into our next section, which deals with motor movements.

6. Motor Movements.

That general physical ability in motor movements is a definite factor in social adjustment has been shown by Jones (1946a) who also discusses sex differences (1947) and skeletal maturing as related to physical ability (1946b). A general test of motor fitness has been developed at the University of Indiana (Bookwalter, 1943), and by Scott and Wilson (1948) for college women. More widely known, perhaps, is the *Oseretsky Test of Motor Proficiency* for children (Lassner, 1948) which is being widely used at present. Malmo and Andrews (1945) discuss a recording device for foot tapping which they consider to be sensitive in detecting slight impairments in motor performance. Liefmann (1945) shows that physical performance is related to mental ability in school in 152 girls. Fisher and Birren (1946) have standardized a test of hand strength.

The linking up of studies of this type with work on expressive movement on the one hand and psychiatric classification on the other should lead to advances of our understanding in this field.

Mirror tracing is a motor skill which has been studied intensively by Loutitt (1943), who finds significant correlations with emotional instability, the unstable taking longer and performing more poorly on the task than normal groups. Similarly, Wechsler and Hartogs (1945) draw attention to the use of mirror drawing as an aid in the clinical measurement of anxiety. Brower (1948) correlates mirror drawing scores with personality traits and cardiovascular activity, and Telford and Storlie (1946) relate respiration and reflex winking rates to muscular tension during mirror drawing learning. The relation of learning to personality is also suggested by Masucco (1945), while the individual's preference for speed or accuracy in working has been shown to be related to temperament by Himmelweit (1946).

7. *Level of Aspiration.*

Research on the level of aspiration technique has been summarized by Lewin and others (1944), but since then several important discoveries have been made. The level of aspiration technique gives essentially two scores. Using a test in which the subject can only guess rather vaguely what his future or past performances will be, or have been, he is asked before the performance to give a quantitative estimate of what he hopes to achieve and after the performance to give a quantitative estimate of what he has achieved. He is then told his actual achievement and the process of aim setting and of judgment of past performance is repeated before he is told the actual score on a subsequent performance. In this way, a number of "level of aspiration scores" are accumulated, calculated as the difference between aspiration and achievement, and similarly, a number of "judgment scores" are obtained, defined as the difference between actual performance and the subject's quantitative estimate of how well he actually thinks he has done. An additional score is the "rigidity score," defined as the tendency of the subject to cling to one particular level of aspiration, irrespective of his actual performance.

Eysenck and Himmelweit (1946), Eysenck (1947*b*) and Himmelweit (1945) have shown that hysterics tend to have a low level of aspiration, to over-rate their actual achievement and to be lacking in rigidity; anxiety patients and other dysthymic types of personality, however, have high levels of aspiration, tend to underestimate severely their own achievements and frequently show a high degree of rigidity. Normal persons tend to be intermediate between these clinical extremes. Ax (1946) reports results of similar import. Other results relating the level of aspiration to personality are given in a study by Hanawalt and others (1943) of 20 leaders and 20 non-leaders; Klugman (1948) in a study of emotional stability and level of aspiration; Gruen (1945) working with adolescents; Klugman (1947), who correlated level of aspiration scores with other tests; Rotter (1945), who analyzed different patterns of response; Preston and others (1947), who studied the dependence of level of aspiration on the difficulty of the task, the amount of information available, motivation and the realism of aspirations, and Holt (1946), who studied the problem of whether the level of aspiration records the ambition of a subject or is a defence mechanism. His conclusion that the more aspirations diverge from realistic predictions, the more defensive the behaviour of the subject, agrees well with the finding that anxiety states tend to have quite high levels of aspiration.

8. *Aesthetic Preferences.*

The relationship of aesthetic preferences to personality tests has been hypothesized by many writers in the past; a history of experimental attempts in this field is given by Eysenck (1947*b*), who showed that hysterics and anxiety patients are differentiated significantly by their preferences both in the field of aesthetics (landscape paintings) and in the field of humour. Barrett (1947) studied preferences of women for colour or tint and showed that women who preferred colours gave fewer answers to stimulus words and higher annoyances scores, were more masculine and changed their minds on social and economic matters less frequently than other women who preferred the tints. Those

preferring colours were judged to respond more directly and with greater interest to objects and objective events. Rakshit (1946) reports that subjects tested as extroverts preferred deeper colours than introverts. Franck (1946) investigated the personality correlates of preferences for sex symbols and came to the conclusion that girls preferring male symbols were more mature, accepting the female role better and accepting men as their counterpart more frequently than girls who preferred female symbols.

Also in this section belong studies on preferences for colour or form in tests which make it possible to lay greater stress on one or other of these two factors. One such study is reported by Tuompo (1942), who finds that popularity is related to colour preference and unpopularity to form preference, a result which ties in well with the previous findings of Kretschmer (1926), Enke (1928), Schaefer (1927), Lindberg (1938), and others, regarding the greater form preference of the schizoid and the greater colour preference of the cycloid types. Campaillia (1943) contradicted these well established findings and showed a higher number of colour reactions in a group of schizophrenics than in a group of normals, and an accentuation of this colour tendency as the seriousness of the disorder increased. Eysenck (1947*b*) also reports findings suggesting a greater degree of colour reaction among the more abnormal and finds no correlation between colour form reaction and different types of neurotic disorder. It seems likely, therefore, that if Campaillia had used a manic-depressive group, in addition, this group would have been even more colour reactive than the schizophrenics, thus bringing his results into line with the usual findings.

In addition to work on these more strictly aesthetic types of material, studies relating to sense of humour would also seem to belong in this field. The work of Eysenck (1947*b*) has already been mentioned. Cattell and Luborsky (1947) and Luborsky and Cattell (1947) report on a factorial study of humour preferences and the correlation of the resulting clusters with scores on the Guilford-Martin Personality Inventory and an intelligence test. These findings are interesting and suggest the possibilities of constructing more analytic tests of sense of humour than we already have.

9. *Perseveration.*

Work on perseveration has recently been summarized by Cattell (1935) and Eysenck (1947*b*), who also shows that tendencies to extremely high or extremely low perseveration are correlated with neurotic instability. Collins (1948) found negative correlations between intelligence and perseveration, while Misiak and Pickford (1944) found a correlation between body build and perseveration, showing that leptomorphic boys tended to be low and eury-morphic boys tended to be high perseverators. Walker and others (1943, 1945) discuss the relationship between perseveration and the concept of mental inertia, and the influence of scoring methods upon scores in motor perseveration tests.

10. *Rigidity.*

The original work by Kounin on rigidity (1939, 1941*a*, 1941*b*) has been criticized by Werner (1946) and expanded and defended at length by Kounin

(1948), while Luchins (1947) discusses rather different methods for the measurement of this concept. It is unfortunate that most of the work in this field has been done on mental defectives because here, it would appear, we have a method of approach eminently suitable to the study of many mental abnormalities.

11. *Perceptual Tests.*

A test resembling the Bender Perceptual Gestalt Test is reported by Gislock (1940), who worked on 70 mental patients and 10 normal controls. He concludes from his work on the reproduction of designs that disturbances of perception, in the strict sense of the word, do not exist, and that the error in the reproduction usually occurs during the motor action and not during the perception, thus contradicting Bender's (1938) view, which emphasizes the perceptual element. Yacorzynski and Neymann (1946) studied 40 normal, 30 manic-depressive and 30 schizophrenic patients with an 8-figure completion test. They also lay stress on the fact that in visual motor tests of perception the effect of the motor element has to be considered in addition to the perceptual factor. The authors conclude that the responses of the schizophrenics showed a decrease in motor activity; those of the manic-depressives an increase. These findings should be read in relation to work on expressive movement and the autokinetic phenomenon, summarized above. Another perceptual test is reported by Angyal (1948) consisting of short-time exposures of simple letter combinations. She interprets her results in terms of two main types: those showing indications of a loose personality organization and those showing signs of a rigid personality organization, contrasting on the clinical side the anxiety states and hysterics to the obsessive-compulsive neuroses. Results from these well-structured tests should be compared with the rather poorly structured perceptual tests of the Rorschach type, to be discussed later.

12. *Frustration Reaction.*

The concept of the frustration threshold (Sherman, 1947) is based on the reaction of subjects to frustrating experiences. Neurotics appear to have a very variable and low threshold; normals tend to be more consistent and have a higher threshold, while that of schizophrenics appears to be highest of all. Rosenzweig (1945) also interprets his results in terms of increased frustration tolerance with increasing integration of personality. Other studies in this field are those of French (1944), dealing with the reaction of organized and unorganized groups to frustration; Wright (1943), dealing with the influence of frustration upon the social relations of young children, and Miller and Bugelski (1948), relating frustration to aggression. Further studies are collected in a volume by Lewin and others (1944).

13. *Pain Reaction.*

Pain sensitivity in normal and neurotic patients has been studied by Chapman (1944), who concludes that pain perception of psychoneurotic patients does not differ significantly from that of normal control subjects; he found, however, that there was a tendency for hysterics and anxiety states to react

to a weaker stimulus than the patient suffering from hypochondriasis. Schilling and Müsser (1948) studied 71 neurotics and 138 non-neurotics. Their results are also largely negative. The apparatus used in this experiment is described by Hardy, Wolff and Goodell (1943). Wolff and Goodell (1943) also discuss the pain threshold in relation to analgesics, placebos and suggestion. Chapman, Cohen and Cobb (1946) confirm the general finding that pain perception of the heat stimulus will not differentiate between normals and neurotics. They also find, however, that the level at which the neurotic reacts to the heat stimulus by wincing or pulling away is lower than for normals. This finding would seem to link up these experiments with those on persistence, already reported. Thompson and Gellhorn (1945) link up muscle pain with the electrical resistance of the human skin, indicating some generalization of discharge in the sympathetic nervous system.

14. *Psychogalvanic Reflex.*

Changes in the electric conductivity of the skin have been studied by a large number of authors. In the main, interest has been in the technical improvement of the apparatus and the method of scoring the results of this test. Blank and Finesinger (1946), Haggard (1947) and Lacey (1947) may be mentioned in this connection. Duffy and Lacey (1945) interpret decreasing conductivity as indicating decreasing energy mobilization. Staudt and Kubis (1948) have studied the P.G.R. and its relation to changes in tension and relaxation, while Hoch, Kubis and Rourke (1944), working on 100 psychotics and 100 normals, equated for age and sex, showed that improvement in mental condition is reflected in more normal P.G.R. records. Silverman and Powell (1944) report excessive palmar sweating by means of a colorimetric technique; they found excessive sweat reactions most frequently in patients diagnosed as psychoneurotic. This finding links up with work on the P.G.R. because of the well known relation between the reflex and palmar sweating.

15. *Flicker-Fusion.*

Much work has been done on the Flicker-Fusion threshold, a test of particular interest because of the report by Krugman (1947) that on comparing 50 neurotics and 50 normals he found considerable differences between the two groups, the anxiety neurotics having a considerably higher threshold than the normal group. Other researches in this field have dealt mainly with the use of the test as a measure of fatigue (Graybiel and others, 1943); the effect of age (Brozek and Keys, 1945); effects of sex (Misiak, 1947) and tobacco (Roussel and Weekers, 1947). This phenomenon is of undoubted interest clinically and it will, no doubt, be developed to a considerable extent during the next few years.

16. *Conditioning.*

The literature on the conditioned reflex, even during the past few years, is far too extensive to be reviewed here, but attention should be drawn to the extremely interesting work by Welch and Kubis (1947*a*, 1947*b*), who show that patients with anxiety neuroses can be conditioned more quickly than normals.

Considerable agreement was shown between degree of anxiety and reaction to the test. Haggard (1943) used the conditioned reflex (P.G.R.) to a strong electric shock in order to establish and "cure" autonomic reactions. His work may be relevant to the evaluation of clinical therapeutic methods and certainly deserves further study.

17. *Respiratory and Circulatory Measures.*

Tests of these physiological concomitants of emotion continue to be used as personality tests by many authors in a variety of experimental situations. Brower reports on respiration and blood pressure in a mirror tracing situation (1946), while Finesinger (1943) discusses the use of the spirogram in certain psychiatric disorders, using a numerical method of scoring respiratory tracings of 250 neurotics, schizophrenics and normals. He also reports (1944) the effect of pleasant and unpleasant ideas on the pattern in neurotic patients, comparing 64 patients with 24 normals. Friedman (1947) describes the construction of a hyperventilation index and its use in assessing and differentiating effects of neurocirculatory asthenic syndromes, while Silverman, Lee and Drinker (1944) describe a pneumotachographic device for recording the velocity of air movement during expiration and inspiration. Ruskin and others (1947) report on electrocardiograph measures of 100 psychotic and neurotic patients, showing a variety of aberrations in the E.K.G. recordings. Van der Merwe and Theron (1947) used the Goetz finger plethysmograph as an indicator of emotional stability, reporting a correlation of .41 between rate of blood volume change and results on the Bell Questionnaire in 30 normal subjects. McCurdy (1947) reports a significant correlation between basal metabolism and success of students at college; he fails to find any correlation between B.M.R. and intelligence score. Kleitman (1945) reports a study of rise of temperature among persons attending a motion picture; an interesting example of a rarely used technique of measurement.

18. *Visual Disorders.*

Livingston and Bolton (1943) and Rees (1945) report on the marked tendency of neurotics to have much greater difficulties than normals in ordinary tests of dark vision, and many other ocular disturbances are discussed in the literature. Thus, Ironside and Batchelor (1945) discuss the ocular manifestations of hysteria in relation to flying; Dunlap (1943) shows a considerable defect in colour vision in mentally maladjusted subjects, and May (1948) finds abnormalities of the pupillary light reflex in schizophrenia, while Miller (1945) shows a considerable amount of correlation between hysteria and corneal anaesthesia.

19. *Body Build.*

Much interest has been shown in the relation between body-build and personality in recent years and a review of much of this work is given by Eysenck (1947*b*) who also reports on results of experimental studies, indicating a marked tendency for hysterics to be eurymorph in body-build, whereas anxiety states and reactive depressives are leptomorph. Neurotics, as a whole, were found

to be more leptomorph than comparable normal groups. Turhan (1940), reports on a study of Kretschmer's types among 230 pupils of a military school. Smith and Boyarsky (1943) related Sheldon's three types of physique to scores on a simple reaction time test, finding endomorphic individuals to have slow and ectomorphic to have fast reaction times. Fiske (1944) also investigated Sheldon's classification and concludes that "the use of Sheldon's improved procedure for classifying physique yields the same paucity of significant relationships that have been found in earlier studies." Moore and Hsü (1946) report a factorial study of anthropological measurements in psychotic patients, concluding that paranoid and non-paranoid schizophrenics really belong to different categories, and also that non-paranoid schizophrenia is differentiated anthropologically from manic-depressive states, a finding in line with the results of Beitz (1942).

20. *Autonomic Functioning.*

Many of the studies reviewed have used tests of autonomic functioning in one way or another. A report by Wenger (1947) has attempted to relate a number of measures of autonomic balance to the hypothesis that indices of autonomic balance are related to emotional and personal-social behaviour. He interprets his findings as indicating a genetic and physiological basis for various personality traits, a conclusion borne out by a study of Jost and Sortag (1944), who investigated monozygotic twins as well as other types of siblings and concluded that autonomic constitution may be, at least, partially inherited. This conclusion is also well in line with the results of Eysenck's work (1947*b*).

SUMMARY.

It seems to the writer that the tests discussed in this section, dealing as they do with highly structured and objectively measured reactions in significant situations, are more likely than any other group of tests discussed in this chapter to lead us eventually to a proper scientific understanding of personality and to enable us to measure its various aspects or dimensions accurately and validly. The large number of significant relations which have been found between different types of personality disorders and such objective measures as speed of conditioning, autonomic balance, flicker fusion, and so forth, suggest strongly that these disorders are closely related to the dysfunctions of the autonomic system and both receptor and effector parts of the central nervous system. In tests of this type, it would appear we are dealing with the bed-rock of human personality rather than with the quicksands of daily mood and quickly changing attitudes, interests and verbal reactions generally.

In view of this, it is encouraging to find that measures obtained in this way are not isolated, but fall into meaningful groups and patterns, as shown, for instance, by Eysenck (1947*b*). Co-ordination of results from this field with results obtained from verbal and from unstructured types of tests must, at the moment, be one of the most interesting research possibilities in the field of psychological test development.

UNSTRUCTURED TESTS.

While psychological tests using unstructured material are not precisely novel, yet their large-scale application has become common only quite recently. These tests fall into four main groups: *Completion Tests*, in which the subject is required to complete a chain of associations, a sentence, or a story, the beginning of which constitutes the stimulus; *Interpretation Tests*, in which the subject has to interpret, discuss, or tell a story about some kind of indeterminate stimulus; *Production Tests*, in which the subject is asked to draw, paint, or, in a play situation, construct or produce some kind of product that can be scored or interpreted, and *Observation Tests*, in which the subject is put in some kind of vaguely structured situation and his behaviour is observed and used as a basis for rating or classifying him. This fourfold division is by no means watertight logically, and there is a good deal of overlap; nevertheless, it will form a useful method of arranging our data.

I. *Completion Tests.*

1. *Association Test.*—Tendler (1945), in a study of the significant features of disturbance in free association, found that such features tend to show low intercorrelations and that combined scores on several of them showed significant differences with respect to psychotics, psychoneurotics and manic-depressives. Meltzer (1943) investigated sex differences in children's attitudes to parents by means of a free-association interview, showing sex differences in notions of parents. Foley and Macmillan (1943) demonstrate differences in associations according to type and amount of professional training. McIntosh (1944) gives evidence of the occupational significance of the contrast response to a free association test. Smith (1945) has investigated the relation of masculinity-femininity scores of sorority girls on a free association test to those of their parents. She finds that "feminine" girls tend to have a more feminine mother and a more "masculine" father. She also finds some slight evidence that the more highly "masculine" man seems to marry the more highly "feminine" woman.

Martin (1945*b*) studied the word-associations of schizophrenics and manic-depressives, finding no meaningful differences between these two classifications, but showed the importance of geographical and individual features. Lang (1943) investigated the use of long reaction time as a complex indicator. Goodenough (1946) and Goodenough, Fuller and Olson (1946) report interesting experiences with a free word-association scale, consisting of 238 homographs, i.e. words which are identical in their written form but have different meanings. Responses can be used as a masculinity-femininity index. Leadership qualities in women are revealed by this test and results indicate that marked non-conformity with reactions characteristic of one's own sex tends to be associated with personal unhappiness or social difficulties. Schafer (1945*a*, 1945*b*) discusses the rationale of word-association tests.

Liberson (1945*a*, 1945*b*) and Liberson and Prescott (1946) used word-association tests, together with an EEG, finding a number of interesting correlations between the two. Ebaugh (1946) reports on the use of a modified Luria technique in connection with word-association tests.

An attempt to objectify word-association tests is reported by Malamud (1946) and by Crown (1947). These authors used a stimulus word followed by two pre-selected responses, one of which has to be chosen by the subject. Normal and neurotic reactions are determined experimentally and item analysis is carried out so that the final test differentiates validly between neurotics (who tend to underline the neurotic response in each case) and normals (who tend to underline the normal response in each case). There is no doubt that this method of administration has great possibilities and will probably become much more widespread. Lastly, an interesting suggestion by Pflugfelder (1945) may be noted. The subjects are required to react to each of 128 initial syllables with a complete word. His published results, however, do not indicate any real superiority of this method over the more usual ones.

2. *Sentence Completion*.—The Sentence Completion Test appears to be considerably more useful clinically than the Word-Association Test. Pioneered by Payne in 1928, it has been used by many people and has been transformed into a standard test by Rohde (1946, 1948). Essentially this test consists of a number of sentence beginnings, such as "I feel proud when . . . ," or "I become disgusted with . . . ," or "I brag about" Reliability and validity of this test seem to be dependent on the method of scoring which may be according to Murray's system (1938) or along rather simpler lines (Rotter and Willerman, 1947). These authors separate responses into three categories—conflict or unhealthy, neutral and positive or healthy responses, getting a 7-point grading for each response. Carter (1947) used an Incomplete Sentence Test in combination with the psychogalvanic reflex, suggesting that it was of value as a means of determining the relative importance of various areas in an individual's emotional life. Symonds (1947), who reports on the use of 100-item Sentence Completion Test in the Assessment Programme of the Office of Strategic Services, concludes that the test is not a safe guide for prediction, although it does seem to reveal anxieties and hostilities. Shor (1946), reporting on a similar test of his own construction, considers it a valuable clinical tool, since it can easily be modified to fit individual needs. Stein (1947) also discusses the clinical use of this test. Tests of this type might, with advantage, be constructed along the lines of the multiple choice objective scoring method, and, indeed, one such use is reported by Cattell (1948).

3. *Story Completion*.—Roody (1945) reports on a plot completion test which consists of 10 plots, each with 5 alternative endings, which have to be ranked in order of their probability by the subject. Two of these endings are possible and highly probable; one is contrary to the facts of the story; one an extraordinary coincidence, and one contrary to nature. The same author (1943) reports an index of reliability for the test of .91 and suggests its use in revealing the subject's attitude towards his own life problems. Taylor (1946a, 1946b) has used completion of two incomplete stories with Indian Students, rating the spontaneous story endings on a 5-point scale on the basis of reality thinking involved. Sargent (1944) has constructed a test of insight into human motives in which the subject has to take a brief story presented to him and answer questions regarding the action of the principal figure in the conflict situation outlined and his feelings. Complex scoring categories are given and certain

maladjustment indicators outlined. Fassett (1948) carried out a study of the test-retest reliability of the Sargent Test, but did not find it very reliable.

There is no doubt that this sort of completion technique has many interesting features which should be followed up and that it may give us a valuable method of clinical investigation.

II. *Interpretation Tests.*

1. *The Thematic Apperception Test.*—The Thematic Apperception Test and its interpretation are discussed in a number of recent books and papers—Zubin and Young (1948), Rapaport (1946), Stein (1948), Tomkins (1947), Rotter (1946), Wyatt (1947), Gough (1948), Sarason (1948), and many others. While this test has also been used as a therapeutic aid by Bettelheim (1947), Arango and Lasaga y Travieso (1947) and others, its main purpose, of course, is as a diagnostic device. As such, it has been applied to psychotic children (Leitch and Schafer, 1947); runaway girls (Gothberg, 1947); head injuries, neurotics and brain injuries (Renaud, 1946); neurotics and psychotics (Wolfenstein, 1944); adult schizophrenics (Balken, 1943); mental defectives (Sarason, 1943); and psychopathic defective criminals (Kutash, 1943). The most careful study to date, is, perhaps, one by Eron (1948), who compared 25 schizophrenics and 25 controls, matched with respect to age, education, mental ability and marital status. He concluded that the results of his study indicated that the thematic material obtained on the Thematic Apperception Test is very much a function of the stimulus properties of the cards themselves and that the specific personality disturbances of the subject are not nearly so important in determining the type of theme that individuals will produce. Every theme which appears in normal subjects is also related by at least some schizophrenics, and in over 100 comparisons made between the two groups, differences were found in only 13 categories at, or beyond, the 5 per cent. level of confidence. A great number of views held without any experimental basis by many practitioners are exploded by this study, such as, for instance, the view that misinterpretation of the sex of some of the persons shown has pathological significance. In Eron's study he found that the normal group showed greater sex misinterpretation than the schizophrenic patients, although this difference was not significant. It is to be feared that many other types of interpretation confidently made on many other "projective" techniques would also fail to find confirmation when subjected to careful experimental studies of this kind.

A number of studies deal with the reliability and validity of the test. Harrison and Rotter (1945) show medium-sized reliability on ratings of emotional maturity and stability on the basis of five of the T.A.T. pictures by two independent examiners. Mayman (1947) reports rather higher reliabilities but used only 11 subjects. Combs (1946a, 1946b, 1947) compared T.A.T. stories and autobiographical materials. Agreement between different analyses is only between 50 per cent. and 60 per cent., and agreement of an analyst with himself when attempting to duplicate his original analysis is only in the neighbourhood of 65 per cent. These are so low as to throw serious doubt on the usefulness of the test. Harrison (1940a, b) used a matching method in

estimating the validity of the T.A.T. and showed beyond-chance success on the whole. Slutz (1941) also used a matching method with some success. The same author studied the reliability of the test by comparing results with those obtained by a somewhat similar set of 10 pictures. He reports that very similar material was produced in both tests.

Bell (1948) suggests that the demonstration of statistically significant variations in the responses of various diagnostic groups to the test is another method of determining validity. This would certainly be true if the assessment of statistically significant variations in these studies were properly carried out. However, in the great majority of studies, elementary statistical errors abound which make any attempt at their assessment difficult, if not impossible. Formulae appropriate when one comparison is made are applied to comparisons between groups in which large numbers of different indices are used, and formulae appropriate for independent indices are used when such indices are obviously not independent but highly correlated. In view of these weaknesses, we can only conclude that evidence on this point leaves much to be desired.

A number of tangential studies may be of interest. Coleman (1947) gave two series of T.A.T. pictures before and after a movie to find in what way it influenced these stories. The outcome of the experiment was negative. Henry (1947) studied T.A.T. reaction of about 1,000 children between 6 and 18 years of age from various Indian tribes and concluded that the test provided data regarding some general features of the respective societies in which the children grew up. Temple and Amen (1944) presented a series of 12 pictures containing situations familiar to young children, in which the central figure was drawn in such a way that it might be interpreted either as a boy or as a girl, the child being asked to complete the central figure by putting on it one of two separate heads, one with a happy expression and one with a sad expression. This technique affords a closer approach to the experimental study of the individual personality and would appear to hold some promise. Loebowitz-Lennard and Riessman (1945) had subjects recall their original fantasies immediately and at the end of three days. It would not appear, however, that this method adds much of interest to the interpretation of the test. Symonds (1945) reports on a study of 42 pictures, especially drawn for work with adolescents and gives normative material from stories given by 20 normal boys and 20 normal girls. Lennep (1930) presents a picture test consisting of 4 coloured pictures and a manual for their use for the investigation of social attitudes.

2. While there is thus no doubt that much activity is being expended on this test, and while many psychiatrists on the basis of subjective impressions seem to place great faith in it, evidence regarding its reliability and validity is inconclusive at best, and certainly does not seem to justify extravagant claims often made for it. One possible way of improving the test may be in the direction indicated by Rosenzweig in his *Picture Frustration Test* (1945, 1947), in which pictures of frustrating situations are presented to the subject and he is asked to supply a verbal reaction to such a situation. Moderate reliability is reported by Clarke, Rosenzweig and Fleming (1947) regarding the various scoring categories, which include extrapunitive, intropunitive and impunitive reactions, as well as obstacle dominance, ego-defence and need persistence.

Rosenzweig and others (1946) give scoring samples to facilitate scoring. The recent publication of this test for general use (Rosenzweig, 1944) will, no doubt, help in securing extensive validation studies, which, to date, seem to be missing.

3. Another test which has been used by some workers in recent years is the Szondi Test (1947; Rapaport, 1941, 1946; Deri, 1946, 1947). This test consists of 48 photographs arranged in six sets, each containing the photograph of a homosexual, a sadistic murderer, an epileptic, a hysteric, a catatonic, a paranoiac, a depressive and a manic, from which the subject is asked to choose the two most liked and most disliked for each set. The theory underlying the test is that personality traits in the subject will determine his preferences and dislikes for these various types. This view is linked up with certain general genetic and biological theories which bear no relation to modern scientific work in this field and the relevance of which to the test itself seems doubtful. Validating data given by Szondi are arranged in such a way as to make any reasonable assessment impossible and no validation studies have been reported from elsewhere. Recent work on this test at the Maudsley Hospital, as yet unpublished, throws great doubt on its reliability, as well as on its validity. It should certainly not be used in clinical work until a great deal more is known about its diagnostic usefulness. Any assessment is made more difficult by the cult which has grown up around this test and which seems to have blinded some clinical psychologists to the complete absence of any validation studies.

4. Also dealing with photographs of faces is the *Character Interpretation Test*, at present in the process of construction at the Maudsley Hospital. Whereas the Szondi is based on the assumed process of identification, the C.I.T. is based on the assumption that the attribution of character traits to individual photographs is based ultimately on a process of projection and, therefore, revealing of the subject's own traits and attitudes. A series of 12 portrait photographs is presented to the subject and he is asked, in each case, to underline from a series of adjectives those most characteristic of the individual portrayed, and to cross out those least characteristic of him or her. Promising differentiations have been obtained on giving this form of the test to normal groups and various groups of abnormal patients. In addition to this objective scoring method, provision is also made for the subject to give a free character description of each individual portrayed, and for the ranking in order of liking of the 12 photographs. Lastly, the subject writes down a character sketch of himself as the best-liked and the worst-liked person portrayed would see him. Data regarding the reliability and validity of this test are not extensive enough to justify its use clinically, but such data are in the process of being compiled.

5. *The Rorschach Test*.—More papers are published on the Rorschach Test probably than on all other non-structured types of tests put together and only very brief mention can be made of the most important developments. Of particular interest has been the recent tendency towards a more experimental investigation of various Rorschach factors. Sarason (1947), for instance, tried to analyse the use of colour reactions in the Rorschach by comparison with performance on the Kohs Block Design Test, concluding that inability

to respond constructively to the coloured Rorschach cards is related to poor performance on the coloured Kohs Block Designs. Goldfarb (1945) has investigated the use of animal symbols in the Rorschach Test by means of an *Animal Association Test*. Zubin and Young (1948) report on the use of the *Levy Movement Blots* which attempt to make an analysis of movement responses, having been specially constructed to evoke this type of reaction. Douglas (1947) reports a tachistoscope study of the order of emergence in the process of perception, relating the perceptual phenomenon observed to the various Rorschach factors. Work along these lines, while as yet not more than suggestive, is likely, eventually, by careful experimental analysis of the various factors leading to different types of Rorschach response, to imbricate this test with less esoteric types of experimentation.

From a slightly different point of view Kimble (1945) discusses social influences on Rorschach records, giving the test twice to 14 students, once in a laboratory, the second time in the social atmosphere of a cafeteria. He finds a striking increase of colour responses in the social situation. Another attempt to modify reactions on the Rorschach is reported by Harrower-Erickson and Grinker (1946) reporting on Rorschach reactions after a stress tolerance test. Chalke (1946) substantiates their findings that the Rorschach Test is susceptible to variation through the influence of superficial external stimuli, and Williams (1947) also shows relationship between Rorschach factors and intellectual control under stress situations. Similar reports are made by Brower (1947c), who correlates Rorschach responses with cardiovascular measures before and after a stress situation, finding significant correlations on 38 subjects, and Freeman and others (1944), who show relationship between Rorschach responses and tolerance of anoxia.

Of particular importance is a study by Muench (1947), who used a battery of diagnostic tests (the Bell Adjustment Inventory, the Kent-Rosanoff Free Association Test and the Rorschach) at the beginning and at the conclusion of a course of non-directive psychotherapy, showing considerable improvement in line with psychiatric evaluation on these tests. He failed to use a control group, but this deficiency has been made good by Hamlin and Albee (1948) and there can be little doubt that experiments of this type will do much to advance interest in the possibilities of the Rorschach Test as a measure of clinical improvement.

Factor analysis has been used in relation to Rorschach responses by Hsü (1947), whose analysis does not seem to be relevant to a discussion of the Rorschach, as only one card was used and no interpretation-scoring was attempted. Of greater importance is a study by Cox (1948), who gave the Rorschach to 60 normal and 60 neurotic boys, equated for age, intelligence and social background. She intercorrelated 49 of the usual scoring categories on this test and through a factor analysis identified three main factors: (1) neuroticism; (2) intelligence; and (3) fluency. Identification of neuroticism and intelligence was by external criteria (normal-neurotic dichotomy; intelligence test). With a normal-neurotic category included as one of the items correlated and the neuroticism factor rotated to pass through the dichotomy, a correlation of .82 was obtained between the factor of neuroticism and the

normal-neurotic dichotomy. This suggests very high validity of the Rorschach Test with respect to the diagnosis of neurotic maladjustment.

Other studies of validity and reliability include Gustav's (1946) correlation of Rorschach scoring categories with an objective inventory, which gave significant results; Brenman and Reichard's (1943) use of the Rorschach Test in the prediction of hypnotizability; Morris's (1943) attempt to use the Rorschach as a prognostic method in metrazol therapy; Swift's (1944*a*, 1944*b*) study of reliability and validity of the Rorschach with children; Clarke's (1948) and Thompson's (1948) correlation studies between M.M.P.I. results and colour and movement responses on the Rorschach, respectively; Swift's (1945) correlation between Rorschach methods of insecurity in pre-school children and teacher and parent ratings (this study gave completely negative results); Garfield's (1947) comparison on Rorschach diagnosis and clinical diagnosis, and Seigel's (1948) study of the diagnostic and prognostic value of the Rorschach Test in a Child Guidance Clinic.

Studies of artists (Roe, 1946*a*, 1946*b*, 1946*c*; Prados, 1944) and of scientists and technicians (Roe, 1946*d*) are of great interest in spite of their rather negative results.

A very large number of studies deal with the comparison of different clinical groups: Psychopathic personality (Linder, 1943; Heuser, 1946); epileptics (Altable, 1947; Zalla, 1947); brain injuries (Aita and others, 1947); psychosomatic disorders (Booth, 1946); homosexuals (Due and Wright, 1945); cerebral concussion and psychoneurosis (Koff, 1946); mental defectives (Abel, 1945*a*; Sloane, 1948; Werner, 1945*a*, 1945*b*; Jolles, 1947); stutterers (Meltzer, 1944); neurocirculatory asthenia (Ross, 1945); enuresis (Goldman and Bergman, 1945); and delinquents (Luke, 1943). While these studies are of some interest, their interpretation is not as straightforward as might appear. Of particular interest in relation to the interpretation of test results of this kind is a paper by Kurtz (1948), who showed that a Rorschach scoring system could be developed based on 42 very successful and 38 unsatisfactory sales managers; this scoring system classified correctly 79 of the 80 persons who were used in developing it. However, when used on a different group, this scoring system showed no relation whatever to managerial success. Many Rorschach workers elaborate a system of scoring for distinguishing groups on the basis of even smaller numbers of cases (occasionally as few as 5 have been made the basis of a separate paper) and it is hardly necessary to say that unless such a system is validated on a group other than that from which it is derived, its value is almost nil. It is unfortunate that this elementary statistical precaution is not observed by most writers in this field.

In addition to the reports on the orthodox use of the Rorschach given so far, there have also been a number of modifications which are of particular interest. Munroe (1945) has discussed some of these in a presidential address to the sixth annual general meeting of the Rorschach Institute. The same author (1945*a*, 1945*b*) has developed a group method of administration which she calls the "Inspection Rorschach," where the qualitative and intellectual features of the test performance are disregarded and only the integration or adjustment of the personality considered. This neuroticism index has been

shown to be significantly correlated with the academic performance of college students and to add considerably to the value of the more usual selection tests. Harrower-Erickson and Steiner (1945) also report on the use of group administration by means of projection on a screen of the Rorschach slides and the securing of written responses. Buckie and Cook (1943) and Linder (1942) have reported adaptations of this technique which have been used by Altus (1948) to compare group Rorschach responses with the schizophrenic scale of the M.M.P.I. Abel (1945*b*) used the test in a Vocational High School for picking out maladjusted cases. Abt (1947) showed a high correlation between group records evaluated by the Munroe technique and personal and social history factors of the subject. This author reports that, with the aid of the group Rorschach, a personality inventory and a psychometric test 86 per cent. of neurotic cases were successfully picked out. Klebanoff (1946) used the group Rorschach in connection with his research on operational fatigue in Army Air Forces' combat personnel.

If the group administration of the test and particularly the inspection technique lead one, to some extent, in the direction of greater objectivity, the use of the Harrower-Erickson Multiple Choice (1943) or the ranking method suggested by Eysenck (1947) make the scoring entirely objective. Both methods depend on the selection by the candidate of certain responses, some of which are typically normal and some typically neurotic. The total number of neurotic responses chosen constitutes the scoring of the subject. Much work has been reported on the use of the Multiple Choice Rorschach. Markey and Zisson (1946), Wittman (1945) and Harrower-Erickson (1943) report that the test succeeds in giving results which differentiate various normal and abnormal groups, but many more authors have found that it failed to do so. Among these authors are Balinsky (1945), Challman (1945), Jensen and Rotter (1945), Wittson, Hunt and Older (1944), Malamud and Malamud (1945, 1946), Blair and Clark (1946), Engle (1946), Lawshe and Forster (1947) and Winfield (1946). It seems clear that the Multiple Choice method of giving the test is highly unreliable and that the ranking method suggested by Eysenck (1947) is superior on this count, giving reliabilities above .8 and showing considerable differentiation between different groups.

Other new developments which are relatively difficult to assess are Munroe's (1946) development of a self-administering form of the Rorschach, Janis and Janis' (1946) use of free association in connection with Rorschach responses, and Levine's use of graphic Rorschach productions (1943).

Lastly, we should also mention the production of two parallel series to the Rorschach blots by Harrower-Erickson (1945) and Zulliger (1941).

III. *Production Tests.*

1. *Painting and Drawing.*—Frequent use has been made in recent years of the drawings and paintings of both children and adults in an attempt to discover underlying dynamics. That it is possible to get congruent results from this method is shown by Munroe, Lewinson and Waehner (1944), who found that the Rorschach Test, graphological analysis, and the interpretation

of spontaneous drawings gave results which were claimed to be in good agreement with each other. A more extensive account of the technique used in this study for the interpretation of art products is given by Waechner (1946). Alschuler and Hattwick (1947) give an account in two volumes of the relation between painting and personality of 150 children between the ages of 2 and 4 years. They examined art products analytically, dealing with the separate factors of colour, line, form and space usage. An earlier account of similar experiments is given by the same authors (1943).

England (1943) reports a study of children's drawings, in which a comparison is made between the work of public school, retarded, institutionalized and delinquent children. Slochower (1946a, 1946b) reports a more detailed investigation of the reproduction of dimension and shape in children between the ages of 5 and 10. Ames (1945) made an analysis of drawing behaviour by a method of completion drawing, which is similar in some ways to the verbal completion test discussed in the previous section. Harms (1946) reports on a line analysis for each of a number of different words. He finds characteristic neurotic forms and distinguishes six fundamental types of formal expression. Taylor (1944) suggests from his study of Indian students that cultural determination plays an important part in the production of drawings. Geil (1944) used the Goodenough "Drawing a Man" Test for revealing male homosexuality, and finds that although not all known homosexuals would project feminine characteristics in their drawings of a man, yet whenever a male subject draws a man with feminine characteristics, it is a highly significant indication of a strong feminine component in his personality structure.

Humphrey (1946), Smith and Humphrey (1946), and Stuart, *et al.* (1947) report results on a rather different type of test, in which drawings are rated as expansive or compressive. Using rating methods developed by Elksich (1945) they show that the two groups of subjects, the expansive and the compressive, differ with respect to their scores on extra-sensory perception tests.

A special type of painting in which no brush is used is reported in detail with full historical discussion by Napoli in his monograph on finger painting and personality diagnosis (1946) and some results are reported by Blum and Dragositz (1947). Some authors have used this procedure not so much as a personality test, but rather as a therapeutic technique. Spring (1935), Fleming (1940), Shaw and Lyle (1937), Mosse (1940). Rosenzweig and Durbin (1945) report work on finger paintings of psychotic patients, as does Napoli (1946, 1947).

2. A combination of drawing and interviewing technique is given in Raven's *Controlled Projection Test* (1944). The most formal test presented in this section is Buck's *H.T.P. technique* (1947, 1948; Landisburg, 1947) in which the subject has to draw a house, a tree, and a person. The method of scoring the resulting productions is complex and discussed in great detail in Buck's *Qualitative and Quantitative Scoring Manual* (1948). No results are available to test the claims made for this test. Hellensburg (1945) reports on a completion test, originally created by Carl Horn, consisting of 12 squares, each containing a number of lines, out of which the subject has to make a picture. Sanford *et al.*

(1943) and Berger (1939) are others who have made use of similar completion techniques which certainly hold out interesting prospects, although, at the present stage, validation seems to be largely lacking.

3. *Play*.—Like painting and drawing, play behaviour has been used both as a therapeutic technique and also as a so-called "projective" test. Howard (1944) links play activity with an interview in his study of fantasy and play interview. Sears, Pintler and Sears (1946) report on the effect of father separation on pre-school children's doll play aggression, and Sears (1947) gives a more general discussion of methodology in relation to play. Robinson (1946) shows that identification in doll play is greater in situations representing the child's own family constellation than in a standard situation. Bach (1946) compares the father fantasies of 20 father-separated children and those of 20 control children in a standardized doll play technique, showing among the father-separated children an idealistic fantasy picture and indicating that the control children stressed the father's aggressive tendencies.

Renaud (1946) compared 31 cases of head injury patients and 16 cases of psychoneurosis in a test requiring them to construct scenes using a standard set of figures. He observed significant differences in the *location* of aggressive scenes, the head injury group tending to locate them in the farthest, the neurotics in the nearest sectors. This tendency was reversed when "nurturance" or "punishment" scenes were considered. This stress on the formal aspects of play was first suggested by Harrower-Erickson (1937). It appears to be a very interesting way of approach.

4. Another play situation test is the so-called *World Test*, suggested originally by H. G. Wells in a book on floor-games and developed by Charlotte Bühler and G. Kelley (1941), who made it into a standardized test situation consisting of a box of 150 miniature wooden toys representing people, animals, houses, trees, fences, cars and so forth, out of which the subject is asked to construct whatever he likes. Bolgar and Fisher (1947) have developed a scoring system for this test for adults, using 232 pieces in their equipment. This test also is used both for the purpose of therapy and for the purpose of diagnostic testing (Lowenfeld and Maberly, 1946).

5. A similar test was recently developed by Shneidman, under the title of the *M.A.P.S. Projective Personality Test* (1947). This consists of 21 background pictures printed achromatically on thin cardboard and 67 figures. The subject is required to select some of these cut-out figures and use them against one of the different backgrounds (a ballroom, a cave, a dream-cloud, etc.). Having constructed his picture, he is required to make up a story about it on the lines of the Thematic Apperception Test. This combination of picture and story (hence, M.A.P.S.—Make-A-Picture-Story) is a combination of play technique and the Thematic Apperception Test, which appears to be promising and which has been used by Shneidman (1948) in a study of 50 schizophrenics and 50 normals, carefully matched with regard to age and I.Q. The results of this comparison are significant on a large number of points and result in interpretations which leave little doubt that this test has great value for the investigation of abnormal personalities. Follow-up studies and work on reliability of interpretation are urgently needed before a more definite statement can be

made. In one report, Fantel and Shneidman (1947) link up the M.A.P.S. Test with psychodrama in a purely impressionistic way, without attempting to evaluate one against the other statistically.

Possibly, Psychodrama Technique should also be mentioned in this section, seeing that Atterbury (1945) and Del Torto and Cornyetz (1944) describe its use as an expressive and projective test. However, too little evidence is available to judge the technique and its value in this connection; its main use would appear to be in the therapeutic field.

IV. *Observation Tests and Techniques.*

Observational techniques, interviews, ratings, time-sampling and sociometric devices still form an important part of the psychologist's equipment and certainly belong in the unstructured group, although they can, of course, be arranged in such a way as to be at least partially structured. Particular interest in the use of these devices has been aroused through their use and development in the selection of officers (O.S.S. Assessment Staff, 1946); of civil servants in Great Britain; of clinical psychologists in the U.S.A. (Kelly and Fiske, 1948); of trainee executives (Taft, 1948); and of other professional groups likely to be in leadership positions. Many of these methods were developed by Simonait in his book on *Wehrpsychologie* and were later taken over by the British War Office Selection Boards (W.O.S.B.) and the American Office of Strategic Services. Some of the different methods used for testing the various qualities required of officers, executives, and so forth, will now be briefly described.

1. *Sociometry*.—A very large amount of work has been done in the field of sociometric testing, particularly in relation to leadership behaviour (Jennings, 1943; Van Dusen, 1948; Northway, 1946a); of popularity (Bonney, 1947; Smucker, 1947; Frankel and Potashin, 1944; Reilly and Robinson, 1947; Kuhlen and Lee); of compatibility and friendship (Austin and Thompson, 1948; Bonney, 1946a; Smith, 1944; Zeleny, 1947); and of the social relations between people in various situations (Morgan, 1946; Hartley, 1946; Fieandt, 1946; Bonney, 1946b; Loomis, 1946; and Dwyer, 1947). Detailed instructions for the use of the test are given by the National Committee for Mental Hygiene in Canada (1946) and some general discussions are given by Moreno and others (1943) and Northway (1946b). Suggestions regarding statistical indices for use in the application of the test are given by Criswell (1946), Forsyth and Katz (1946), Zubin (1943) and Findley (1948).

Many of these studies strongly reinforce a conclusion arrived at by Fraser (1947) who found in his interview study of over 3,000 adult workers that "a decrease in social contacts was a circumstance most commonly associated with neurosis." In a similar way, sociometric studies appear to show a relationship between popularity, leadership position, and friendship formation to emotional maladjustment and "neuroticism." Unfortunately, objective measures of neuroticism and other personality traits (apart from questionnaires) have seldom been used in conjunction with sociometric appraisals; this field would seem likely to be productive of interesting and important relations.

2. *Interview*.—Less formalized than the sociometric technique is the interview, which has given rise to some interesting work, in addition to the study

by Fraser, already mentioned above. Of great importance is a study by Chappell and Lindemann (1942) and Chappell (1946). These authors make an analysis of the interaction between interviewer and interviewee in terms of amount of time during which either of them, both, or neither, are actually engaged in talking, and show interesting relations between personality and scores on this test, which certainly deserve to be followed up. Raimy (1948) studied the frequency of self-reference in counselling interviews and found consistent differences between cases which had been counselled successfully and those counselled unsuccessfully. Wittson, Hunt and Stevenson (1946) and Curtis and Thorne (1945) discuss the use of brief standardized psychiatric interviews for screening purposes, indicating that they have considerable usefulness, while Dunlap and Wantman (1947) show that group techniques may achieve as good results as brief interviewing methods.

Of particular interest in this field is the work of Stuit (1947) and of Flanagan (1936), who show that in many military selection procedures, selection by means of statistically weighted tests is superior to selection based on interviewer judgment, although the interviewer has all the test results available to him. These large scale studies are of great importance as they demonstrate fairly conclusively that the often repeated claim in favour of interviewing techniques as serving some kind of "integrating" function are unjustified and that the interview actually detracts from the optimum prediction given by means of the proper statistical combination of scores.

3. *Ratings*.—Personality ratings have been used on a considerable scale by R. B. Cattell (1944, 1945, 1947), Moore, Stafford and Hsü (1947), and Stafford and Hsü (1947), all of whom report factorial analyses of their ratings, as do Brogden (1944) and Tschechtelin (1944*a*, 1944*b*). Hewitt and Jenkins (1946) make an analysis of 500 case records of children in child guidance institutions, resulting in three well-defined syndromes—unsocialized aggressive behaviour, socialized delinquency behaviour and over-inhibited behaviour. They also show typical environmental influences associated with these groups.

A psychiatric rating scale of some interest is reported by Malamud, Hoagland and Kaufman (1946) and a revision of the same by Malamud and Sands (1947). Some data on reliability and validity of rating scales are given by Remmers (1946), Shuey (1943), Weinland (1948), Bonney (1943) and Green (1948).

These ratings are mainly made in retrospect, as part of clinic techniques. Another type of rating is that introduced in the officer selection studies already mentioned, in which the candidates are put into certain experimental situations; for instance "leaderless group" tasks, discussion groups, leadership positions and so forth, and their behaviour rated after careful observation. An excellent description of these techniques is given in the book, *Assessment of Men* (1948), which verbalizes some of the extravagant claims which have been made on the Continent, in England and in America also for this type of approach. The general outlook of those who have carried out this method of assessment is "organismic," by which appears to be meant an approach to the problems of personality which follows the Gestalt line of thinking; a "global" approach which disdains to resort to analysis. Published accounts of the American work fail to supply any data to validate such claims to superiority; indeed,

the follow-up validity coefficients are low to very low. In this country little validation was carried out during the war in the field of officer selection by means of these methods; analysis of data reported since in a variety of unpublished documents indicates that these methods have reliabilities lower than are usually taken as minimal for individual prediction; that different observers differ consistently in their ability to forecast success or failure of the candidates at O.C.T.U.'s; and that the usual orthodox detailed statistical analyses of data can improve predictive accuracy to a considerable extent over and above the "organismic" or "global" kind of impression. Use of such "atomistic" devices has led to considerable improvement in the validity of officer selection.

SUMMARY.

As Bell (1948) has pointed out in his excellent book on projective techniques, tests based on unstructured material should serve two main functions; one of these is the offering of rapid, valid and reliable means by which a clinician may arrive at a picture of the personality of a subject; the other the facilitating of personality studies in psychological research. It is probable that tests of this type are more successful in the first of these two objectives than in the second, although it is extremely difficult to give any kind of objective assessment of the validity or the reliability with which they perform their task. Undoubtedly, they are subject to a number of criticisms, such as lack of standardization, failure to provide acceptable evidence of reliability and validity, faulty statistical treatment of data, failure to control the bias of the examiner, failure to devise objective and universally acceptable scoring systems, and the failure to divorce test results from theoretical systems, such as the Freudian or the Jungian, which, themselves, are lacking in validity. It is often pleaded that these are the faults of youthful exuberance and that with time they will be outgrown. When it is realized, however, that the Word Association and the Rorschach Test, to take but two examples, are not much younger than group tests of intelligence, and when one takes into account the large number of research papers devoted to these tests, it would appear that the fault is not so much one of youth as of general approach. Many users of the so-called "projective" techniques regard them as a kind of philosopher's stone, not subject to the ordinary laws of science, while, at the same time, claiming scientific respectability for their findings.

GENERAL SUMMARY.

It is impossible to evaluate in general terms the different types of test discussed in this chapter. Testing methods are expanding at a remarkable rate in all directions and there can be little doubt that the quality of work is improving at a slower rate than its quantity. Very many claims are made for particular types of test (notably the so-called "projective" and "organismic" techniques) but attempts to justify these claims are made mainly on the theoretical level; actual experimental demonstration of these alleged superiorities or virtues is shirked. The main problem in all validation, namely, that of finding an adequate criterion, is not seriously faced by psychologists, who

simply attempt to validate their tests by correlating them with clinical diagnoses; this procedure assumes clinical diagnoses to give the ultimate scientific pattern of personality structure, an assumption which psychiatrists themselves would be the first to dismiss as over-optimistic. Even if it were accepted, the methods used for testing the various techniques against psychiatric opinion are often faulty. The matching method, to take one example, has many pitfalls of improper identification on extraneous bases which are disregarded by most research workers.

There is one tentative generalization which, while it cannot be regarded as firmly established, may yet provide a heuristic hypothesis to serve as a basis for structuring the very confused files of modern personality tests. It is widely agreed that personality rests on a firm hereditary basis, but is also subject to great alterations through social and other environmental influences. It would appear, by and large, that personality tests of the objective performance type are related rather more closely to the inherited pattern of a person's conative and affective traits; tests of conditioning, of suggestibility, of autonomic imbalance, of sensory dysfunctioning and of motor expression appear so closely bound up with the structural properties of the nervous system and with the body-build or the sensory equipment of a person that the likelihood of hereditary determination can hardly be gainsaid.

On the other hand, tests employing unstructured material would appear to reflect more the historical aspects of a person's life story and be subject to day-to-day fluctuations of mood and outlook. If we may use an analogy from physics we might say that tests of this type deal with problems of hysteresis rather than with those of structure.

If this be true, it can be seen immediately that tests of both types are of value in the clinical situation. Tests of the first type give us information, as it were, about the inherited potentialities of the subject and set bounds to the possibilities of psychiatric improvement; the latter type give us a picture of the subjects' present clinical position and through them we may investigate his previous history and follow the course of his improvement. While this general distinction is not claimed to be an absolute one, it may, nevertheless, prove useful in the assessment of the contribution which different types of tests can make in the study of personality.

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PSYCHOPATHOLOGY.

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AGGRESSION.

DURING and since the war much has been written on aggression, individual and collective, and many conflicting views have been expressed. As is well known, Freud postulated a death, destructive or aggressive instinct to counter-balance a life, creative or sexual instinct. Just as catabolism masters anabolism with physiological death, so the death instinct aims at a return to the inorganic state. Freud's application of this theory to the causes of war and of collective aggression resulted in a pessimistic view for the future of civilization. Since he developed his theory of the death instinct in the years following World War I, it has been suggested that his outlook was to some extent determined by the very bad conditions in Austria during those years.

Recent analytical writers have been more inclined to stress the importance of early training, and some think that aggression could be directed largely or purely into cultural channels. Glover (1947) believes that a fundamental change should be made in the family, for the human mind can only be moulded during its period of relative plasticity. He finds in the nursery all those features in miniature which go to form an anxiety-ridden culture. He states that "flogging, imprisonment and the psychological equivalents of capital punishment should be abolished from the nursery. Bullying and intimidation of children, the compulsory imposition of grown-up codes of convenience, in fact most of the reactionary artifices which go under the misleading label of 'good upbringing' might be restrained." The pacifist movement having its roots in the family tradition would spread to larger and larger groups. It would then be necessary to mobilize the pacifist forces of these larger groups to "play them off against the State." The cultural authority of the family should be extended, and the spurious cultural authority of the State curtailed.

Menninger (1944) also finds that the causes of aggressive behaviour are to be looked for within the family circle. He particularly blames the mother. We are told that her unsublimated destructive impulses have been denied to her child the natural expression of its sexual desires. The mother is as she is because she has been frustrated in a man-made civilization, but this civilization is as it is because man's training had been mismanaged by the mother. It is believed that this vicious circle can be broken if the aggressive urges are harnessed to Eros and directed into socially acceptable activities.

Perls (1947) differs from the psycho-analysts in that he postulates two fundamental instincts—hunger and sex. He denies an instinct of aggression, which he believes to be a very powerful instrument of the hunger instinct, and should have its natural outlet in the use of the teeth. The use of the teeth is

the foremost biological representation of aggression. If this tendency remains ungratified, it may evince itself in such harmful ways as killing, waging war, cruelty, or by means of "retroflexion," as self-torture or even self-destruction. From the foregoing it is not surprising to find that Perls thinks that much could be done to promote good relations, personal and international, if people took exercises in chewing. If people do not dissipate their aggression and lust for destruction by chewing their food, they will find an outlet as a character feature.

Cohen (1946), though he borrows much from the psychoanalysts, is still more indebted to Pavlov. He finds practically no place for innate mental tendencies. The infant mind is a *tabula rasa* which can be moulded by conditioning, training, example, education into exactly what is desired. More particularly aggression is not an innate tendency. Cohen draws support for this from various fields. In the animal kingdom aggressive animals are so by nurture, not nature—that is, they copy the behaviour of their parents. As evidence of this it is found that kittens conditioned to live with rodents kill rats less frequently than cats not so conditioned. The same conclusion is reached by a study of primitive man, namely, that aggression, either individual or collective, is not due to genetic but to cultural agencies. The causes of mass aggression having been established, the remedy is a simple matter and is dismissed in a few paragraphs. The ultimate aim being world-organization, the child's education should be directed towards this end. He should be conditioned against all nationalistic beliefs, competitive behaviour and aggressive activity. The following especially would be excluded: stressing individual excellence and attainment, competitive examinations, the award of special prizes and athletic contests. On the other hand, co-operative and democratic tendencies alone would be encouraged.

While there is some conflict of opinion as to whether aggression, individual or collective, can be eradicated, it seems to be generally agreed that it would be a good thing if it could be done. It is suggested here that it would require the pen of a Swift or Voltaire to do justice to the citizen of the World State as he is depicted by some of the above-named writers.

ANOREXIA NERVOSA.

In four cases of anorexia nervosa, weight changes were found to be the resultant of the caloric intake and energy output, which were influenced considerably by anxiety and resentment. Anxiety was manifested physiologically by a change from a slow pulse to tachycardia, and decrease in glucose tolerance without characteristic changes in appetite. Observations on the metabolism of various dietaries gave no evidence of a "primary" metabolic disorder. The balance of energy changes was similar to that seen in inanition. During most periods the intake of calories was abnormally low, but even with a diet which would have been adequate for the average normal person weight could be lost because of muscular over-activity induced by anxiety (Small, S. M. and Milhorat, A. T., 1943).

Eissler (1943) finds that there are three degrees of anorexia nervosa, depending upon the severity of the condition. In the first degree the condition is

symptomatic of hysteria, melancholia or schizophrenia. The symptom does not reach a dangerous stage in these patients. The third degree is regarded as a disease entity; the symptom-complex dominates the clinical picture, and is not symptomatic of a neurosis or psychosis. Further, the disease entity is found to be associated with a certain group of character traits. These include: specific attitude to food, preponderance of oral traits, an incapacity for appropriation and a certain type of dependence on the mother. Cases of the second degree present a rather indeterminate and unsatisfactory halfway house between the other two degrees.

ANXIETY.

From his experience with service cases, Symonds (1943) is of the opinion that the anxiety neuroses of war include two kinds of affective disorder, which may occur singly, though more often in combination. In one type, that described by Freud, the anxiety is the result of emotional conflict with the frustration of an instinctive urge. In Symonds' opinion this conflict is not always at the unconscious level, as is maintained by many psychotherapists. The second type is due to over-stimulation of the fear mechanism, and results in a state of anxiety out of proportion to the cause. "It is conceived simply as a disturbance of function in that part of the mind, or at that physiological level, which is concerned with the generation of affect." The view would seem to be that natural fear may generate morbid fear in those with an inherited predisposition, and that the two forms of fear have only a quantitative difference. This state of morbid fear may be precipitated by cerebral injury, infection and intoxication as well as by psychical factors, such as the danger situation. It is further pointed out that the latter theory would bring the anxiety states into line with the other affective disorders, states of depression or elation. Many will be inclined to dispute the truth of the statement that the affective disorders can occur without psychological conflict; others will feel that this very difficult subject has been plunged into too lightly without definitions or criteria. In 1926 when Freud summarized his general conclusions on this subject in "Inhibitions, Symptoms and Anxiety," he was very careful to define exactly what he meant by such terms as the danger-situation, objective fear, normal and neurotic anxiety.

Cameron (1945) made an interesting approach to the relationship that exists between anxiety on one hand and excitement and depression on the other. Many clinicians will agree with Cameron that frequently the diagnosis of a depressive or anxiety state is a purely arbitrary one. Again the old neurological grouping of manic-depressive psychosis and the anxiety neuroses is often found to be too schematic. Cameron conceived the affective states as a series, which may be compared with Mapother's schizophrenic-paranoid series. States of excitement, anxiety and depression have in common the fact that the total tensional level is raised. "In the excitements facilitation is maximal and inhibition is greatly reduced, though still present. In the depressions inhibition is present with facilitation greatly reduced. In the anxiety states there is an increase in both facilitation and inhibition, the two, as it were, competing against each other and being responsible for the characteristic picture of curbed

overactivity. On this basis it is possible to recognize a range of reactions : predominant facilitation (manic excitements), facilitated anxiety states, inhibitory anxiety states and predominantly inhibitory states (depressions)." The great advantage of this concept is that it does away with the idea of a hard and fast dividing line between psychosis and neurosis.

AMNESIA STATES.

Parfitt and Gall (1944) provide a general review on psychogenic amnesia based on a study of 30 cases, of whom 20 were complicated by fugues. Their first point is that care must be taken to exclude the possibility of organic amnesia, and it is noted that mixed cases are by no means rare. As a rule the organic type is concerned more with a failure of registration and retention ; the psychogenic type with recall. Again, as a generalization, the psychogenic type is more selective, and is more likely to be limited to personal problems.

Following Gillespie, two varieties of psychogenic amnesia are isolated, the hysterical and the emotional. Hysterical amnesia is an attempt to escape the consequences of an action ; the patient does not forget, he refuses to remember. The process is conscious or near conscious, and there is no need to postulate the concept of dissociation in considering this symptom. The difference between hysterical amnesia and malingering is only one of degree. By far the majority of patients showed a constitutional predisposition to hysterical reactions, while in all cases the amnesia followed a severe emotional upset. As a contributory cause fatigue was present in some cases.

For the second type of psychogenic amnesia the authors prefer the term "defensive." It is an escape from the memory of an intolerable experience. It is admitted that in both types the same mechanisms are at work and, as far as can be seen, the differentiation is made on the fact that, having nothing to gain by disclosing the memory loss, there is no complaint of amnesia in the defensive type. A differentiation of clinical type based on the presence or absence of social gain does not seem a valid distinction. A similar criterion, equally unsatisfactory, is that a rich man's theft is kleptomania. Again it is surprising to learn that there is no need to postulate the concept of dissociation. While it can be agreed that some cases of "refusal to remember" are conscious, and others "near conscious," it is suggested that yet others, to use the authors' terms, are "less near conscious." However, degrees of consciousness and the concept, dissociation, are only indirectly related, the presence of the latter not necessarily implying diminution of the former. By dissociation is meant some failure of synthesis ; the integration of the ego is less than normal. There are all degrees of this failure, from the type of man who expresses scientific views on six days of the week, and on the seventh contradictory religious opinions to the extreme degree of schizophrenic dissociation, and it is hard to see why the minor manifestations of dissociation should be ignored. Though some 20 cases presented fugues, the authors have nothing to offer on the psychopathology of this very interesting condition.

In a paper on fugue states and pathological wandering Stengel (1943) adds a further 11 case-reports to his previous valuable series of 25 fugue states. Case 35 is reported in great detail and is of exceptional interest. This patient

had kept a diary for about four years; extracts from this interesting document described the experiences and feelings of the patient during a fully developed fugue, with the impulse to wander, as well as the mental condition from which the symptom arose.

Regarding the psychopathology of the condition, the new material supports Stengel's previous findings, though in this paper his views are further elaborated. It is found that, though fugues with the impulse to wander occur in a variety of psychotic conditions, there was a tendency to depressive reactions of the constitutional type in all the observed cases. Further, the impulse to wander always emerged from a state of depression, or from a mixed state with depressive and hypomanic features. A practically constant causal factor was a serious disturbance of the home life during childhood, in about half the cases the absence or loss of a parent.

While admitting that hysterical mechanisms are at work in the fugue state, Stengel cannot agree with those who regard the condition as one of hysterical conversion. He points out that: "Apart from the fact that powerful constitutional factors of a kind not operative in conversion hysteria play a part in the aetiology of fugues with the impulse to wander, it is doubtful whether one should classify a certain type of impulsive behaviour as a conversion symptom only because it has a symbolic meaning, and appears to serve the purpose of overcoming emotional tension." Stengel finds that at the unconscious level the fugue means suicide, and he also finds that from time to time these patients had had suicidal thoughts. He notes that recent investigations by Palmer and Reitman suggest that the environmental conditions in childhood increasing suicide proneness in adult life are the same as those operative in the aetiology of the fugue. As to why the same environmental conditions contribute in some cases to the origin of wandering states or vagrancy, in others to the increase of suicide proneness, and in yet others to the development of delinquency, Stengel's answer is that these problems require further research; however, in the case of the fugue his studies have demonstrated that abnormal environmental conditions in childhood become pathogenetic only in co-operation with other aetiological factors.

Fisher (1945) presents six cases of fugue, and his material supports the conclusion that the state of "awareness of loss of personal identity" is preceded by the fugue. For Fisher the individual in a fugue is really a dreamer acting out his dream. He is indulging in acts and fantasies which are in conflict with his super-ego, and the formation of the fugue is to permit the carrying out of these acts and fantasies. The fugue is preceded by a phase of increasing anxiety. The patient is in a situation in which he can neither escape from an anticipated or imagined danger nor fight against it. His solution is an escape from consciousness. In contradiction to Janet's opinion, two of Fisher's patients experienced hallucinations in the fugue state.

Geleerd, Hacker and Rapaport (1945) conclude that fugue states can come about only if the reality anxiety equals or outweighs the super-ego anxiety, or if the outwardly projected super-ego is very permissive. The elimination of the super-ego sets free the counter-catharsis that maintained the repression and the formerly repressed fantasy, then seizes control of consciousness

under a different form of ego organization. The previously conscious part of the ego or super-ego is now repressed by the split-off part of the ego. The former state of affairs is usually re-established when the outside situation has lost its importance, and the function of the fugue state is fulfilled. It is stated that the super-ego in fugue states behaves in a manner similar to that in compulsion neurotics, and the writers found that psychological tests in all their patients showed a predominance of compulsive features. This is in contradiction to the generally accepted view that the fugue is a phenomenon of hysterical dissociation.

Studies of the more drastic degrees of dissociation, giving rise to multiple personality, are infrequent in the literature. Therefore Lipton's very careful and detailed report (1943) on such a case is a valuable addition. The patient, a woman aged 25, was admitted to hospital as a result of a fugue state. Her father and brother had both been in a mental hospital suffering from schizophrenia. Under hypnosis buried memories of incest with the brother since the age of 10, with the father since the age of 12, and promiscuity, continued after marriage, since the age of 16, were recovered. She believed that her brother was the father of her second child. It is to be noted that the author was unable to confirm any of the above by reference to other members of the family.

For the first three months the patient exhibited amnesic phases, after which her behaviour and condition abruptly changed. She became solitary, seclusive and introverted, experiencing auditory and visual hallucination. It was concluded that the defence of hysterical amnesia having broken down, a schizophrenic reaction had supervened.

At an indefinite date after the onset of the psychotic phase a second personality was noted. This second personality was childish, impulsive, swaggering and amoral. The I.Q. for this personality was only 43, and the sensorium was restricted. The two personalities were amnesic for each other, but the second personality had full memory for incest and other sexual delinquencies. Various incidences, including removing, rearranging and breaking of furniture, etc., recalled by the husband as taking place prior to hospitalization, and at that time unaccounted for, suggested that dissociation had often occurred previously. Later a third personality developed, whose memory continuum partly overlapped the other two.

Regarding the psychopathology, it was found that the patient's hallucinatory experiences were always concerned with her brother, and that it was when these became very intense and persistent that the change of personality took place. Though the patient loved her brother, incest was repugnant to her; splitting of the personality was an attempt to resolve this conflict.

APPERSONATION.

Bleuler described this mechanism as that disturbance of the ego in which something situated in the outside world is attributed to one's own person. For instance, one of Bleuler's schizophrenics had the feeling that he was punishing his enemies with "his thunder and lightning" during a storm. He attributed the events in the sky to his own person. According to Sperling (1944),

who approaches the subject from the psychoanalytical angle, it is easily confused with identification. However, in the former, the ego of the patient is not altered; it is only that the boundaries of the ego are extended. He finds that appersonation is an ego-mechanism, and that as such it may appear as a resistance. It permits the gratification of libidinal impulses with diminished feelings of guilt and diminished castration anxiety. The most frequent motive for appersonation is narcissism. Typical examples are exhibitionists, sadists, masochists and suicides, who are content with vicarious satisfaction.

BODY IMAGE.

Bychowski (1943) has made a careful study of the information derived from psychoanalytical and brain-pathological sources on the complex structure of the body image. He finds that on the organic side the body image possesses very rich representation in different segments of the brain, and that from the psychological angle it has important narcissistic cathexis. He concludes that regression and disintegration of the body image can have a twofold genesis: it can result from organic disorder, or from essentially psychodynamic moments.

Bychowski is more particularly interested in the role of body-image disorder as a part of the symptomatology of the psychoses. In involutional states he finds that body-image disturbance is the starting-point in the clinical syndrome. In women especially there is a feeling of bodily change. This feeling starts in the sphere of function of the sex organs, but may spread to the rest of the body and become the focal point for the genesis of paranoid or of guilt feelings. Such feelings will be elaborated in the clinical picture as delusions and hallucinations. In other cases the disintegration of the body image constitutes the source of most bizarre symptoms, such as exchange of bodies and projection of the body into the environment. Beside biological change, as in the involutional psychoses, the same narcissistic insult may be offered by certain physical injuries or disorders—for example, fracture of the nose, skin diseases and operations, more especially on the eyes or sex organs.

Depersonalization of the whole body or else of some organs may originate in psychogenic mechanisms; then it constitutes a result of partial withdrawal of libido. A similar effect may also be produced by brain-pathological mechanisms. The phenomenon of anosognosia may be linked to such partial depersonalization on a brain-pathological basis. In various hypochondriacal syndromes the disorder of body image plays a predominant role. The problem of total or partial projection of the body image seems to include manifold implications. It ranges from the well-known phenomenon of phantom through projection of non-injured parts of the body, and it ends in total projection of the entire body image (autoscopy).

Brown and Goitein (1943) have attempted to secure pictorial representation on paper of this self-impression of the bodily schema. The subject is told to visualize a mental picture of himself in space and to draw it in outline, keeping the eyes closed. The authors experimented with some 250 individuals, and conclude that this self-impression of the body image throws considerable light on the personality as a whole. It was found possible to determine from a normal population five distinctive types of elaboration and representation of

the body image. These five basic patterns were found to agree fairly closely with specific patterns given by five groups among the psychoses, viz.: cycloid, repetoid, schizoid, hysteroid and paranoid. The diagnosis of the personality type is made on consideration of a number of features in these drawings. Nevertheless it would seem that the actual physique of the subject might be a cause of fallacy in the results. For instance, several drawings by normal subjects are illustrated, and it might be argued that the drawing labelled cycloid was that of a normal subject of pyknic build, and that the drawing labelled schizoid was by a normal asthenic. Against this it could be argued that the body itself, as well as its image, is an indication of the personality type, but this is not hinted at in the text.

Roth (1944) also stresses that the neurophysiological apparatus subserving the function of body imagery is subject to both psychogenic and organic derangement, and that psychogenic problems in this sphere have much more devious ramifications and elaborate superstructures than do those originating in organic cerebral lesions. He thinks that the facts that can be learnt from studies of disorders of the body scheme, caused by organic brain lesions, should help to shed light on the common meeting-ground of organic and functional disturbances of the nervous system. He describes two cases of anosognosia, a symptom-complex not uncommon in functional cases, but here due to organic lesions.

BOREDOM.

Bergler (1945) regards boredom as a disease entity. It is usually the central feature of the neurosis, and is associated with a triad of disturbances. These are weak sublimations, inner inhibition of voyeurism, and defence against masochistic pleasure. Boredom therefore represents an unsuccessful defence mechanism of the unconscious ego against reproaches of the super-ego. The relationship of boredom to depersonalization is discussed. The disease is progressive in untreated cases, and may result in suicide.

CAPGRAS' SYNDROME.

Vie (1944) provides an exhaustive study of Capgras' syndrome and allied conditions. He holds the view that there is an organic basis for the delusional psychosis, upon which the idealistic superstructure is imposed as a reaction of the psyche to a morbid organic process. Of these morbid reactions systematized misidentification is a striking example. Vie believes that the ego in an attempt to safeguard its integrity and continuity is forced to sacrifice social elements one by one. At first there is a refusal to accept the fact that there is a mental disorder. Next there is a misinterpretation of contemporary events vitally affecting the patient. Then there is misidentification or non-recognition of those about the patient. Lastly there is denial of personal identity.

Stern and MacNaughton (1945) present two cases of the syndrome, one a female schizophrenic, the other a male maniac. It is noted as a feature of the syndrome that the person who is experienced as a double is a beloved, who—with the change of identity—becomes at the same time hated. However, the writers believe that there are more basic disturbances at the biological level of the personality, which are causal of the syndrome. They quote Nornicke

and others, who have found that even in the pre-delusional phase schizophrenics complain that subjectively perceptive experiences seem different or modified. For instance a schizophrenic observed, "I was immediately struck by the strange way in which things such as cars and people were moving in the street." These are primary changes of the experience which cannot be defined or reduced any further, and are closely related to "*déjà vu*" and certain types of "psychic aura" in epilepsy.

CONSTITUTIONAL TYPES.

Sheldon and Stevens (1942) provide an important contribution to the study of physical and temperamental types. This work is an attempt to correlate the findings of an earlier work by the same author on *The Varieties of Human Physique*, with three types of "cluster" of temperamental characteristics. The findings of the earlier work are summarized in this volume, and may be briefly epitomized here. In the first place it should be made clear that so far the anthropometric measurements have only been worked out for males ranging from 16 to 21. With regard to these measurements certain diameters are expressed as ratios to stature. The authors have been able to isolate three physical types, which they term endomorphy, mesomorphy and ectomorphy. In endomorphy the digestive viscera are massive and highly developed; in mesomorphy the somatic structures (bone, muscle and connective tissue) are in the ascendancy. Ectomorphy means fragility, linearity, flatness of the chest, and delicacy throughout the body. There is relatively slight development of both the visceral and somatic structures. It will be seen that Sheldon's three physical types closely correspond to Kretschmer's pyknic, athletic and asthenic body builds. It would appear that Sheldon's somatotypes present two advances on those described by Kretschmer.

In the first place Sheldon's types are morphologically more fundamental and less prone to inaccurate diagnosis. For instance some of Kretschmer's pyknics on Sheldon's measurements would turn out to be athletics who have gone to seed. The second advantage is that the method of tabling an individual case allows for a much more accurate total picture. Sheldon's somatotype is a series of three numerals, each expressing the approximate strength of one of the primary components in a physique. The first numeral always refers to endomorphy, the second to mesomorphy, and the third to ectomorphy. When a seven-point scale is used, a 7-1-1 is the most extreme endomorph, a 1-7-1 is the most extreme mesomorph, and a 1-1-7 the most extreme ectomorph. The 4-4-4 falls at the midpoint with respect to all three components.

In this work 200 young men have been analysed both morphologically and temperamentally, and the results are presented. Regarding the temperamental tests a variation on the technique of factor analysis was used. The authors standardized the description of 60 traits—20 in each of three correlated clusters—which collectively made up what appeared to be three primary components of temperament. The first component, termed viscerotonia, is characterized by general relaxation, love of comfort, sociability, conversability, gluttony for food, for people and for affection. It is associated with endomorphy.

The second component, somatotonia, is roughly a predominance of muscular

activity and of vigorous bodily assertiveness. It is associated with mesomorphy. These people have vigour and push; action and power to define their life's primary purpose.

The third component, cerebrotonia, shows a predominance of the element of restraint, inhibition, and of the desire for concealment. They shrink from sociality, "repress" somatic and visceral expression, are hyper-attentional, and sedulously avoid attracting attention to themselves. The somatotype is ectomorphic.

The authors find correlations of the order of about $+ .80$ between the two levels of personality (morphological and temperamental). This work would seem important, since it is capable of fairly accurate statistical verification. On the other hand, so far the correlations only apply to a small age group, and the female sex awaits investigation. Again, though the first two temperamental types have something in common with the cyclothymic and cerebrotonia with the schizothymic type, it is clear that at present the authors have little to offer the psychiatrist to compare with Kretschmer's detailed analysis of morbid type psychology. It is suggested that "psychiatric entities—such as the schizophrenias, the manic-depressive psychoses and even chronic alcoholism—appear to be closely related to dyscrasias or irregularities among the primary temperamental components. It is admitted that in this field observations are preliminary and tentative. However, we are informed that further work is in progress.

Against the above, Lasker (1947) found that in a series of 34 persons who submitted to a partial starvation diet for 24 weeks there was a noticeable change in somatic type, and that the majority of traits changed in most of the individuals.

Eysenck (1944 and 1947) carried out a factorial analysis on the inter-correlations of 39 trait ratings on 700 neurotic soldiers. The cases were unselected except for the exclusion of those in whom physical factors and symptoms complicated the picture. Four factors, one with positive saturations only, the other three with both positive and negative saturations, accounted for 40 per cent. of the variance.

The first, or general factor, neuroticism, contributed 14 per cent. to the variance. It is defined as the "badly organized personality," and is regarded as the obverse of the general factor of integration or "will" discovered by Webb. The second, bipolar factor, 12 per cent., contrasts on the one hand the affective or dysthymic group of symptoms (anxiety, depression, obsessional, apathy, irritability), and on the other, hysterical group of symptoms (conversion symptoms, narrow interests, little energy, sex anomalies, hysterical attitude, low intelligence, no group membership, and unskilled). The third factor, 8 per cent. also bipolar, contrasts items stressing hypochondriacal preoccupations with items of a more psychological type. The fourth factor, 6 per cent., showed a low correlation and is of doubtful significance. It is thought to divide a social misfit group from a psychological conflict group.

The first factor is believed to be related to McDougall's "self-regarding sentiment," Freud's "ego-ideal," Janet's view of "psychic tension," and Pavlov's theory of "strength of nervous functioning." The second factor is

thought to divide the patients into an hysterical and an affective group, and to be consistent with the typologies of Janet, Jung, McDougall, Kempf, Bleuler, Kretschmer, etc. This factor, which lends support to the theoretical views of the typologists, is the most significant conclusion reached by the investigation.

Rees and Eysenck (1945 and 1947), in a second investigation, carried out a factorial analysis on 400 neurotic soldiers. An index of body-type was arrived at, calculated for these patients and correlated with 200 psychiatric trait ratings. This index of body-build showed hysterics to have a higher preponderance of lateral growth, as compared with the dysthymics, who have a higher preponderance of linear growth. The results of this analysis support the view that there are two temperamental types characterized by specific personality traits, specific neurotic disorders, specific body-build and specific autonomic activity. These types are not considered as separate categories, but "as the extreme ends of a normal trait-continuum stretching from the typical representative of the 'hysterical' or 'extraverted' type on the one side, to the typical representative of the 'affective' or introverted type on the other." The authors provide the following table in which the two types are contrasted:

	<i>Introverted type.</i>	<i>Extraverted type.</i>
Body-build	Leptomorph	Eurymorph
Clinical syndrome	Dysthymia	Hysteria
Intelligence	High	Low
Schooling	Good	Bad
Autonomic activity	Unbalanced	Normal
Work record	Satisfactory	Unsatisfactory

When the findings in these two papers are compared with those of Kretschmer, some startling discrepancies come to light. It must, however, be remembered that Kretschmer's findings were based on a study of psychotics, while Eysenck studied "neurotic" soldiers. Regarding body-build both authorities agree that there are two extremes which are associated with certain personality types and clinical syndromes. For Eysenck the eurymorph build is associated with the hysterical or extraverted personality, the leptomorph with the affective or introverted personality. While this does not necessarily contradict Kretschmer, the placing of schizoid and cycloid traits certainly does. Cyclothymic traits are placed well over towards the introverted or dysthymic group, and, according to the second paper, tend therefore to an asthenic build. Schizoid traits are found near the mean, but inclining towards the hysterical, extraverted eurymorph type. Five hundred out of the 700 were found to show cycloid or schizoid traits, so that it cannot be said that the two traits were infrequent, and therefore this specific finding unreliable. Again, it is mentioned that the ratings were made by over a dozen psychiatrists, "all different in their theoretical leanings." A pronouncement of such a body of opinion from such an important centre deserves very particular attention. It is, to say the least of it, surprising that such a discovery, which shakes Kretschmer's theory to the roots, should pass without comment in the text. Again, factorial studies to

estimate degrees of suggestibility produced the surprising result that hysterics were less suggestible than dysthymics.

Rees (1945) also undertook an anthropometric investigation of 200 soldiers suffering from effort syndrome. This revealed that the group as a whole was significantly more leptosomatic in body-build than a comparable control group.

Comparison of the aetiological factor in the leptosomatic and pyknic effort-syndrome groups showed striking differences, indicating marked constitutional predisposition in the leptosomatic group, as shown by family history, long-standing symptoms of effort intolerance, negative disequilibrium, hypochondriasis and general neuroticism. In the pyknic group the syndrome was usually of short duration, determined mainly by exogenous factors, and there was little evidence of constitutional predisposition.

A statistical survey of 2,000 neurotic soldiers was carried out by Slater (1943). In his opinion there is a generalized predisposition towards neurosis, which is in large part responsible for the appearance of neurotic symptoms in the individual when placed under stress. This constitutional tendency, though it may be affected by such environmental factors as early processes of conditioning, is at least in part dependent on heredity factors. It is further believed that the constitutional tendency varies inversely with the degree of stress under which the individual is placed before breakdown occurs. In a further paper (1944) he supports the theory that the neurotic constitution is preponderantly determined by a very large number of genes of small effect. In so far as the effects of the genes are qualitatively similar, they may be additive. In so far as they are qualitatively dissimilar, the type of stress effective in producing breakdown, and the neurotic symptoms produced, will tend to differ.

Dicks (1947) criticizes Slater because of the importance he assigns to organic damage and the primacy of constitution. He states that Slater regards constitution as an unalterable, structural, static matrix, on which events act mechanically as conditioning forces. He also complains that Slater slurs over a great mass of psychoanalytical experience with these few words: "Psychological and physiological conditioning produced by the environmental circumstances of the past." To the present writer it would seem that what Dicks really objects to is the determinism implicit in Slater's theory. Once it is allowed that behaviour is the inevitable result of environmental and constitutional forces, it would seem that there is ample room for all the mechanisms of Freud, the psychotherapeutic activities of Dicks and the physiotherapy of Slater.

Symonds (1943) made a survey of flying personnel suffering from functional nervous disorder. In his series more than two-thirds had a family or personal history of neuropathy—that is, a predisposition to neurosis. He also found that the degree of stress required to cause a nervous breakdown was in inverse proportion to the degree of predisposition.

DÉJÀ VU.

Pickford (1944) gives examples of *déjà vu* from the auto-biographical writings of Tolstoy and Proust. These illustrate the psychoanalytical theory

that *déjà vu* is due to infantile or very early memories or impulses of special emotional importance. Objective circumstances or stimuli provide the associative lines. The experience *déjà vu* is felt when these buried memories attempt to break through the surface of consciousness.

DEPERSONALIZATION.

Shorvon (1946) investigated 66 cases of depersonalization. He found that the onset is practically always sudden, and usually occurs in adolescence or early maturity. It may be a symptom in a very wide range of psychiatric disorders. It may also occur in normal people as a fleeting experience, for example, in fatigue, after an anaesthetic, and experimentally during mescaline intoxication. It is a reversible condition, and cases can recover completely and spontaneously. The author also finds a significant relationship to migraine and to obsessional traits. The onset is significantly related to relaxation following intense or prolonged stimulation, psychological or physical. The symptom can be experienced in the cognitive, affective or conative field. More intelligent people, as well as emotionally immature subjects, are especially liable to experience the symptom. There is a high incidence of unsatisfactory parental-child relationship, and there is a higher incidence of non-specific mild abnormality in the E.E.G. of this group than many other groups except deteriorated cases.

On the negative side it is found not to be a disorder of visual perception; it cannot be accounted for in neurological terms; it is not related to any anatomical brain disease; there is a relative absence of olfactory, gustatory or auditory derealization; it is extremely rare in children, and is practically never found in paranoia.

DREAM INTERPRETATION.

Lowy (1946), a pupil of Stekel, provides a psychobiological approach to dream interpretations. In his opinion the dream is a representation of the whole ego, as a psychosomatic unit. He believes that the conceptions of Freud, Adler, Jung and Stekel are by no means in true contrast to one another; rather they are complimentary. Lowy gives particular attention to somatic stimuli in dream formation, previously neglected in favour of psychic causation. It is held that there is a need for a unified conception of the total dreaming process, which would consider the two kinds of dream-stimuli as having a common denominator. The manifest dream, as a conceptualized and verbalized event, arises at the subconscious level. Below this are the deep dream-processes, the real source of the manifest dream. These are non-conceptual, affect-energetic events, arising at a level where psyche meets soma. It is believed that the normal functioning organ bombards the brain with nervous stimuli, interpreted by the psyche as affect, and that this is the normal contribution of the organ to dream formation. The over-stimulated organ, physiologically or pathologically, produces an overdose of affect, and the simultaneous stirring up of associated complexes. Dreams are cited as being determined by peristalsis of the overloaded stomach, bronchitis impeding the breath, toothache, fever, the urinary urge, erection, pollution, etc. Unlike the

Freudians, dream-gaps, dream distortion and symbolism are held to be due to the inability to conceptualize or verbalize many of the dream processes, which are either unthinkable or can only be represented symbolically.

ENURESIS.

Stalker and Band's investigation (1946) is based on a study of 67 cases of enuresis in adolescents and adults. Psychiatric abnormalities were found in the majority of patients. The most frequent were anxiety and psychopathic states, but other types occurred. It was noted that the same lack of inhibitory control was found emotionally and socially in the behaviour of enuretics. The electro-encephalographic and cystometrographic findings linked enuresis with personality in its fullest neuro-psychiatric sense. Constitutional aspects were further shown by predominance in the male sex, associated automatic disorders, especially heavy sleep, by the serious family records of psychiatric conditions and of enuresis. Psychopathological causes before the age of three were shown to exist. They were so numerous and serious as to appear almost as important as the constitutional factors. Abnormalities of breast feeding were especially frequent. It is concluded that enuresis is not just a symptom, but a disease in itself, the total personality being involved in its constitutional, neurophysiological and emotional aspects. The writers find that there is little evidence that it is due to local overactivity of the spinal micturition reflex, but the beneficial effect of large doses of ephedrine might suggest this.

In an unselected sample of 25 delinquent children Michaels (1943) found a total incidence of enuresis in 52 per cent. and of persistent enuresis in 44 per cent. The author believes that there is a relationship between persistent enuresis and delinquency—"both being expressions of some common fundamental disorder in the psychopathic personality."

Thorne (1943) noted that nocturnal enuresis persists into adult life much more commonly than is generally recognized. Of 1,000 consecutive selectees at an Army induction station 16.1 per cent. reported enuresis after the age of 5; 2½ per cent. did not gain control until aged 18 or later. Associated nervous or mental symptoms were noted in 63 per cent. of the bed-wetters. A study of 369 mental defectives revealed enuresis in 83.8 per cent. of 54 idiots, in 12.8 per cent. of 164 imbeciles, and in 4 per cent. of 125 morons. The view is taken that frequently nocturnal enuresis is a sign of a developmental defect which will disappear spontaneously when maturation within the central nervous system is completed. Since the incidence tends to decline with increasing age, it is likely that any form of treatment will be crowned with success in due course. Against this generalization there is the fact that many children who have acquired continence often develop enuresis without organic cause. In these cases it is often possible to associate the onset of the enuresis with some emotional trauma.

Levine (1943) studied 150 cases of enuresis among naval recruits. He also thinks that it is not a clinical entity, but a manifestation of a deep-seated personality disturbance. Other symptoms of a neurotic nature, such as somnambulism, nightmares, nail-biting and nervousness, were often present. He finds the bed-wetter to be usually an immature personality type, and notes

that there is frequently a family background of psychiatric abnormality. He inclines to the view that insecurity, due to the presence of large families, home disruption, poor economic and social conditions and neurotic parents is the most common cause of the condition.

FOLIE À DEUX.

Gralnick (1943), who has previously published an important paper on this syndrome, in which all the published records in English are reviewed, here provides a very detailed study of this clinical entity as it occurred in four members of a family. The mother is the inducer, exerting an evil influence on her weak-willed husband and very dependent children. Faced with two alternatives, to regard this woman as insane or to accept her delusions, all three take the easier line of following her into the realm of unreality.

Gralnick's example illustrates clearly that isolation of the family from outside contact is favourable to the development of *folie à deux*. It also supports the contention that bad socio-economic conditions are a fertile ground for the development of the condition. His main hypothesis, that all psychoses, and *folie à deux* in particular, are primarily a sociological rather than a biogenic problem, can be accepted only with reservations.

Kesselman (1944) presents a case of *folie à trois*, in which there is a paranoid situation involving three persons living in close relationship with each other. It is atypical in that the primary agent is the youngest of the three persons involved.

Kallmann and Mickey (1946) hold that it is advisable to qualify the original and clearly delineated definition of *folie à deux*, which restricted the application of the term to the transference of circumscribed delusions in closely associated persons. The additional restrictive qualification is that similar delusional syndromes should not be called "induced" or *folie à deux* if they appear in units of blood relations, and if the primary significance of blood relationship cannot be safely excluded. This point is amply illustrated by a series of case-histories in which it is made clear that heredity and not induction is the important aetiological factor.

Adler and Magruder (1946) present the cases of identical twin sisters, aged 26, who developed a state of schizophrenic excitement with paranoid ideas on the same day. One sister was the leading influence, and the other was regarded as an induced psychosis. Besides the common constitutional predisposition, there was a high degree of identity of environmental influences and a similarity of symptomatology. Both sisters reacted promptly and favourably to electric shock treatment, after separation had failed to produce an improvement.

GRAPHOLOGY.

Eliasberg (1944), noted that there are two developments in graphology. The older is character graphology, the most recent is a technical branch concerned purely with the recognition and identification of handwriting on the basis of isolated marks. The author thinks it unfortunate that these two developments should have drifted apart.

The science of graphology takes it as an axiom that "there is a psycho-physical correspondence and particularly a motor and spatial symbolism corresponding to the emotions and character traits." There are, however, a number of factors, such as moods, acute emotion, alcohol, disease, fatigue, change of work, life crises and sociological causes which may alter the handwriting, so that it has been said that it is impossible to have a science where the object continues to change.

Medicine may use graphology for the diagnosis and prognosis of disease. Besides the psychoses, graphology is of value in cases of cancer, tuberculosis, rheumatism and pathological ageing. Especially it makes for a better knowledge of subjective factors, particularly the adjustments of the patient to his disease.

Stainbrook and Lowenbach (1944) studied a series of patients undergoing convulsive therapy. They were asked to write their names or simple sentences, both before and at various time intervals after electrically-induced convulsions. "The first letters of writing after convulsion may give evidence of tremor and motor inco-ordination, but all the outstanding characteristics of the individual's ordinary handwriting were seen from the earliest performance onwards, both in the formal aspects of the letters and in the general manner of writing." Regression was shown by the use of childhood pet names, etc., phonetically simpler spelling and perseveration. At first the writing is also more expansive and space-filling than normal. An orderly and consistently occurring pattern-sequence of the motor functions of writing is seen in the recovery from the convulsions. Experiments were also carried out using Wertheimer's original Gestalt figures.

Marum (1945) provides graphological reports on the temperamental qualities, character and intelligence of 50 neurotic subjects, and compares them with the psychiatric records. The two agreed very closely as regards psycho-neurotic traits, which included depression, anxiety, obsessions, hysteria, epilepsy and psychopathic personality. There is a brief description of the pathographical characteristics of these conditions. On the other hand, there was not a satisfactory correlation between the graphological assessment of intelligence and the matrix test.

The study of character graphology in children presents special problems. Schryver (1944), described a test suitable for children, and she found the handwriting analysis of value in revealing emotional tendencies, inhibitions, neurotic features and intellectual abilities in a series of children between the ages of 7 and 12.

The following paper by Rottersman (1944), on the use of green ink does not strictly belong to this subject. The writer found that of 34 males using green ink, in 16 cases the reason was fortuitous. The other 18 used it for preference, and of these 50 per cent. were rejected for military service by the psychiatrist as against the usual 15 per cent. among literate selectees. Psychiatric investigation showed that "males who chose to use green ink, taken as a group, appear to be dependent on their mother, or mother substitute, many marrying women older than themselves." The use of green ink is an attempt to express their individuality or independence.

HALLUCINATIONS.

Eidetic imagery is closely related to visual hallucinations. Kao and Lyman (1944) review the literature since the pioneer work of Jaensch, and also report on a psychotic woman, aged 31, whose delusional system was based on eidetic imagery. An eidetic can mentally project the image of an object at will and with sensory vividness. The faculty is not confined to the sense of vision. Eidetic vision is a primitive and undifferentiated type of vision; it is found in children and primitive races as well as in psychopathological subjects. It is found that quite a proportion of schizophrenics have some type of eidetic imagery, and it is thought that as the disease develops, so the faculty is uncovered. It is not clear if there is a direct relation between eideticry and schizophrenia, or between this capacity and hallucinations. The case reported was not hallucinated, but, depending on the definition of the term, pseudo-hallucinations may have occurred.

HYPNOSIS.

Kubie and Margolin (1943) conclude that the hypnotic state is one of partial sleep, "in which active sensori-motor channels are restricted to those between the subject and hypnotist." This state induces hypnagogic reverie, in which vivid sensory memories and images are released. These in their turn open the way to buried memories, especially those charged with affect.

PATHOGRAPHY.

During the period covered by this survey there have been a number of interesting pathographical studies. Marie Konstantinova Bashkirtseff, the Russian writer and artist, is the subject of a paper by Christensen (1943). He attempts a psychoanalytical interpretation of her personality based upon the "Journal," and to some extent upon an interpretation of her paintings. This study reveals "a regression to infancy, jealousy masking homosexuality, exhibitionist tendencies, masculine traits, a narcissistic emphasis on all parts of the body, and a preference for white and red." There is evidence of sado-masochism, which is thought to be derived from an experience at the age of three. Penis envy and an inverted Oedipus complex are also clearly indicated. Bashkirtseff is, of course, the unknown correspondent who fascinated Guy de Maupassant. It is curious that Christensen makes no reference to these delightful letters; they certainly bear out his findings.

Johnson (1943) studied that macabre poet of dirges, Thomas Lovell Beddoes. The following biographical matter is considered significant: the early death of the dominating, aggressive and eccentric father, the early genius of the poet, the rapid exhaustion of creative power, the change from poetry to science, alcoholism, the homosexual episode, suicide.

From the psychoanalytical angle he is a homosexual with anal-sadistic traits, who identifies himself with the father, and for whom the sexual act means death. For the analytical psychologist he is primarily an intuitive-feeling type, a side of his personality which he continually attempts to smother. For the psychiatrist he is a cold, rigid schizoid incapable of finishing anything, "a poet of fragments." The early creative barrenness suggests a schizophrenic

process, though excessive alcoholism may have been an added factor. Numerous quotations illustrate Freudian symbolism and schizophrenic thinking.

Evans (1943) holds that Puritanism, the most repressive religious movement in history, has left an indelible stamp on the English character. This being so, it is worthy of careful study. The method chosen is by means of a psychoanalytical investigation of the character and conversion of John Bunyan, a typical representative of the movement at its inception. The process of conversion is shown to follow along orthodox lines: the vision, conviction of sin, absolution, a sense of mission. At the personal level there is ambivalence towards the father, but, after conversion, Bunyan adopts a feminine attitude towards the father-image, God, with repression of sensuality which is identified with the bad father, the Devil. At the social level the good father is Cromwell, the bad the Crown and the free-living Royalist leaders. Bunyan and the Puritans have as their aim religious, commercial and political liberty. With the overthrow of the Crown it is true that these were largely obtained, but only at the expense of severe deprivation and restriction of liberty in other directions. The sacrificed king is the father image, the penalty for blood guilt severe sexual taboos, with taboo on sensual pleasure in general. In fact sexuality can only find indirect expression at the anal level, and the paper concludes with a detailed study of the characterological peculiarities of the average middle-class Englishman of to-day: his moral athleticism, his methodology, his integrated system of reaction-formations, his snobbery and social ambition, his compulsion to doubt, and his ceaseless activity, which finds its most congenial expression in the world of commerce and finance.

Charlotte Brontë's biographers have tended to explain her mental sufferings as having been determined by external causes, "the treatment she received from a harsh and cruel father, the loneliness and bleakness of the West Riding landscape, the sadism of her teachers, or the horrible life she had to lead in her situations as a governess." Friedlander (1943) brings forward evidence to show that these mental peculiarities were due to psychological conflicts dating back to early childhood.

At the deepest level there is identification with the elder sister, Maria, a substitute for the dead mother. There is evidence that Maria suffered from enuresis, and that, in Charlotte's opinion, she was punished in a harsh and excessive manner by the school-teacher, and that this persecution caused Maria's death. These events "revived an old masochistic phantasy of great intensity, probably connected with Charlotte's relationship to her mother, and the struggle against yielding to this phantasy seems to have been at the root of her constant unhappiness." There is repetition of this masochistic attitude and hostility towards women in each new situation, and the complex is a central theme in the novels. With the masochism are combined father-fixation and penis envy. The writer finds this combination by no means rare, and that it always gives rise to a typical and interesting personality.

Smith (1943) shows that Aaron Burr's character and career correspond to the oral type of personality, more particularly the oral optimist. An attempt is made "to trace some of the genetic origins of the recusancy and political renegation for which Aaron Burr was ostracized by his contemporaries and damned by

posterity. From these same oral determinants derive as well the contradictory characteristics of generosity, courage, affection and good humour, the gayer, more lovable side of his personality."

Wight (1944) shows that the various phases through which Picasso's art passed, though apparently random and disconnected, have a logical and inescapable sequence. Space forbids a précis of the analysis of "La Vie" and allied paintings, the Harlequins, acrobats, brooding women and the "still-lives." The cubist pictures are explained as being a defence mechanism, which for years protected the artist from his infantile emotional life. It acted as a grill which Spanish etiquette placed between the lovers who were left alone. However, in the later cubist pictures, "The Three Musicians," etc., there is a return of the repressed, the screen taking on the characteristics it is intended to conceal.

Lastly Harris (1946) provides a study of the epilepsy of Dostoevski.

Of more recent work in pathography Halliday's "Mr. Carlyle My Patient" is of outstanding interest. It is a psycho-somatic study of what the author rightly calls "the most famous stomach in literary history."

PHOBIAS.

Fenichel (1944) brings forward evidence to show that in the phobic person anxiety-producing sensations are projected into the phobically endowed object. He especially emphasizes the importance of the fear of overwhelming inner excitement as a source of anxiety in the phobias. He goes on to explain that in an adult ego the idea that excitement is necessarily dangerous emerges only when satisfaction is frustrated by endogenous obstacles, that is, by fear of castration or loss of love.

PSYCHOANALYSIS.

Psychoanalysis, like orthodox psychiatry and unlike some other schools of psychotherapy, is strictly deterministic. Certain popular physicists, as a result of recent findings in quantum physics, have lent their support to the libertarians. This is by no means the viewpoint of all physicists. Wisdom (1943) argues that "physicists predict to a high degree of probability upon a statistical basis, and that this procedure is simply one that does not use the concept determinism." The fact that it is not used by physicists does not mean that it is not true in nature, or that it is unnecessary to apply it in psychology. The factors favouring the concept determinism are twofold; the results of scientific experiments are continually supporting it and, for most minds, an uncaused event is inconceivable. The case for libertarianism is that man has an intuition of freedom of choice, and morality presupposes its existence. Regarding the second, Wisdom thinks that less attention would have been given to the matter if the choice was always at the conscious level, that is, at the level of reality-thinking. What the libertarian requires is free will to control personal pleasure at the id level when it conflicts with moral duty. It is possible for the libertarian to be reconciled to determinism on this point if it is understood that more than often the forces of the super-ego are stronger than those of the id, and that therefore determinism is quite compatible with a man's power of acting from "higher" motives than mere pleasure. On the intuition of freewill it is noted that we all tend to identify ourselves with our "higher" motives; the "basal" ones are in some way extraneous to ourselves.

Gerö (1943) attempts to show that in the neuroses and in certain psychoses, the so-called psychogenic psychoses, psychogenesis is a valid and scientific concept. For the psychotherapist of whatever school it is a fundamental hypothesis that at least certain disorders are psychologically motivated, and are therefore amenable to psychological treatment. The writer, it is clear, has thought deeply about this subject, and has tried to avoid some of the pitfalls. In so doing some may think that he has only succeeded in cutting the ground from under his feet. Most will agree with the writer that a "traumatic experience" is the common lot of mankind, and cannot be considered as the essential cause of a psychological illness; at best it can be looked upon as a part of the causal chain. This applies whether the trauma is in adult life or infancy. Turning to psychological conflict, it is rightly considered that this hypothesis is the most important of Freud's discoveries. Again it is noted that conflict is not the peculiar property of the abnormals, for we all have the experience frequently. It is then explained that what is peculiar to the abnormal is not the psychological conflict or conflicts provoked by traumatic experiences, it is the pathological reaction or mechanism which he uses in an attempt to resolve this conflict. Forced logically to explain why a pathological mechanism should be used, a constitutional factor, hereditary predisposition, is at last admitted.

If the psycho-analytical theory of man's ontogenesis is accepted, it is only logical to accept at least on broad principle Freud's phylogenetic theory on the origin of society and culture. Psychologists will probably agree that the theory as set out in 'Totem and Taboo' is, from the psychological angle, more acceptable than any theory so far provided by professional anthropologists. Unfortunately the theory has gaps; Freud was the first to admit it, and it remains little more than an ingenuous speculation. Daly (1943), who has already published on this subject, notes especially that Freud leaves out of consideration very largely the role of the mother, mother deities, exogamy and the taboo on menstruation. In his latest paper Daly has made use of recently acquired advances in our knowledge of sex physiology, more particularly the relationship between "heat" and menstruation. In the light of this he has been able to correct some errors in his former papers.

Briefly, Daly holds that, following the breakdown of the horde phase, the community enforced severe sexual restraint on the individual members, particularly on the sexual activities of young males and females. These penalties were so severe as to produce finally a breach in the steady evolution of the sex instinct, so producing the so-called latency period between 5 and puberty. Daly points out that this retardation of sexual maturity only takes place in man, and that even in man there are examples of atavism (menstruation, conception and birth of a viable child at the age of 5 to 6 have been reported). A further peculiarity of man, again differentiating him from the rest of the animal kingdom, is the fear of menstruation, the most virulent of all the taboos. Daly notes that in animals in the first stage of "heat" with bleeding that, although the female does not permit copulation, the female is, nevertheless, attractive to the male. It is a phase of fore-pleasure in which many senses participate. In man these positive feelings have been replaced by disgust and repulsion. Daly finds that this is because of the connections of blood with oral and sexual satisfaction on the one

hand, and the fear of death and castration on the other. It is also thought that the menstruation taboo provides a clue to the solution of incest dread and ambivalence towards the female genitals, which Freud thought to be a result of castration fear.

PSYCHOSEXUAL ANOMALIES.

Jonas (1944) does not regard homosexuality as a disease entity. He believes it to be a manifestation of poor personality integration, and would place it in a similar category to excessive masturbation and chronic alcoholism.

In a genetic survey of psychic impotence Bergler (1945) found that the various manifestations of psychic impotence may be due to regression to the phallic, anal or oral level.

At the phallic level the unconscious reason for the different types of hysterical penis neuroses is unsolved attachment to the mother of the Oedipal period, with subsequent repression of the sexual desire for her, identification of all sexual objects with her and persistence of castrative fear.

At the anal level the obsessional neurotic regards everything sexual as dirty and therefore taboo. The chronic hypochondriacal neurasthenic and the perverted masochist are also considered to regress to this level. On the oral level penis and breast, vagina and mouth, sperm and milk are unconsciously identified. The outer world is equated with the "refusing" pre-Oedipal mother.

In a contribution on fetishism Wulff (1946) has collected together a number of cases of fetishism in infancy and early childhood. It is pointed out that Freud's explanation of castration fear could not apply in these cases. Wulff notes that the young child makes use of the fetish chiefly before falling asleep, and directly in connection with thumb-suckings. She concludes that the fetish, through its odour, its pleasant warmth and the particular ductile sensations it produces, is a substitute for the maternal body, particularly the breast.

PSYCHOSOMATICS.

Fenichel (1945) attempts a classification of psychosomatic phenomena. He distinguishes four classes of organ-neurotic symptoms:—(1) Affect equivalents: In this class anxiety, sexual excitement or other affect may be blocked out of consciousness and supplanted by sensations in the intestinal, respiratory and circulatory apparatus. (2) In this group the unconscious affects result in changes in the hormonal state of the organism, experienced as painful feelings of tension and unmotivated emotional attacks. (3) Physical results of unconscious attitudes or of unconsciously determined behaviour patterns. (4) Combinations of these three possibilities.

Bennett (1946) gives a detailed analysis of 150 patients, in whom an illness basically psychic was not recognized until it developed into a grave psychiatric syndrome. Multitudinous faulty treatments over many years for symptoms attributed to organic disease in every bodily system were traced. When at last these patients were treated under a psychiatric discipline, relief often resulted in a short time. Regarding surgical interference, it was found that the 150 patients had shared 244 operations.

Harrington (1947) states that the precision of diagnostic and therapeutic

procedure in ophthalmology has led to a conspicuous neglect of psychic factors in ocular disease. Just as in other bodily systems, prolonged but reversible physiological disturbance can eventually give rise to irreversible organic disease. Vasomotor disturbances, glaucoma and hysterical manifestations are described and discussed.

Simons and Wolff (1946) investigated 63 cases of chronic post-traumatic headache. They concluded that save for headache associated with subdural haematomata and subarachnoid haemorrhages, the chronic headache results from sustained contraction of the skeletal muscles of the head and neck. These contractions are associated with sustained emotional stress, though they may be augmented by noxious stimuli arising from abnormal healing.

Ross and McNaughton (1945) compared the Rorschach findings of patients with migraine headaches with those suffering from psychogenic headache, headaches of unknown origin, miscellaneous psychoneurotic symptoms, brain tumour or injury, and symptom-free individuals. They concluded that the migraine subjects have some features in common with psychoneurotics and others in common with organic brain disease. In a further paper Ross (1945) studied a series of patients suffering from neuro-circulatory asthenia against controls. The Rorschach showed that these patients tend to give up easily in the face of difficulties, and that they are obsessively conscientious.

Ruesch (1945) investigated the psychophysiological relations in cases of head injury. He found that the post-traumatic syndromes without signs of brain damage resembled the psychoneuroses more than the post-traumatic cases with evidence of brain lesions. He concluded that there exists an antagonism between the presence of brain damage and psychoneurosis. The more marked one component, the less obvious the other.

Patterson and others (1943) have found that in a series of rheumatoid arthritics emotional stress produced a drop in skin temperature indicative of changes in circulation. It is thought that the tendency to a prolonged disturbance in circulation secondary to emotional stress may have some influence on the course of the illness, or in inducing exacerbations. They conclude that the importance of emotional factors and their method of action remain undetermined, but that there is sufficient evidence to justify further investigation.

Ripley and others (1943) studied a series of patients with diseases involving the muscles. It was found that emotional changes often were accompanied by altered performance of the muscles; that psychopathological findings were of importance in those cases in which the symptomatology was in excess of the physical basis and that in such cases the condition could be improved by psychotherapy.

Wilson and others (1943) studied a series of cases of organic nervous disease, including post-encephalitic Parkinsonism, multiple sclerosis, pseudo-sclerosis, dystonia musculorum deformans and brain tumour. In their series they note the following: Initial symptoms followed emotional disturbance or psychic trauma; at first the objective neurological signs were minimal. It is suggested that emotional trauma precipitates both physiologic and psychologic alterations, which lead to the appearance of objective neurologic signs. In this series of cases the time relation between emotional trauma and onset of illness is certainly striking.

A psychosomatic study by Pollak and Kreplick (1945) showed peptic ulcers in 42 out of 2,000 necropsies on mental patients. More than half of the ulcer patients were emotionally unbalanced before the outbreak of their insanity. There was little or no evidence to show that there was a causal relationship between the personality type, emotional instability, psychoses and the ulcer formation.

Squier and Dunbar (1946) discuss the psychosomatic approach to pregnancy. They believe that correct psychosomatic management of the mother may influence the early development of the infant.

Roth (1945) reviews the neuropsychiatric aspects of porphyria, basing his conclusions on a study of 10 cases. He found that the disease occurs with special frequency among people with severe neurotic personality disorders. The patients are usually of the hysterical type, except where organic brain disease masks the personality disorder.

SLEEP DISORDERS.

Jekels (1945) believes that in sleep the ego disintegrates, and that sleep is closely related to and is synonymous with death. He identifies the periodicity of sleep and wakefulness with the pattern of the incomprehensible cosmic process which produced life out of lifeless matter. He agrees with Ferenze's statement that "sleep represents the repetition of bygone forms of existence; even of the form of existence before the origin of life itself."

Davidson (1945) divides disturbances of sleep into two main categories, conditions of insomnia and hypersomnia. In this paper he only deals with those of his cases which were of psychogenic origin. He finds that in the neurotic sleep disturbances caused by psychic stimuli the patient is largely dominated by profound repressions. These create conflict and tension and a wish to avoid or solve the conflict. Psychoanalysis has shown several specific responsible factors, which include repressed sexual wishes, desire for omnipotence, death wishes, and the guilt feeling arising from them.

Davidson in this same paper presents two cases of Narcolepsy. Both were of organic origin, but emotional factors were also of importance. Davidson's experience supports the view of Simmel that an attack of narcolepsy may symbolize the passive experience of the death of the patient as a retribution for a death wish against a hated parent or parent-substitute.

Davidson and Demuth (1945-6) are here mainly concerned with the anatomical and neurophysiological disturbances of the sleep mechanism. Regarding psychogenic disturbances, they believe that sleep is a retreat in order to avoid the unpleasant features of reality and powerful and perverted instinctual drives. In some cases this retreat is resorted to in order to obtain gratification.

Pai (1945) studied 117 male adult neurotics in whom sleep-walking and other sleep activities were predominant symptoms. Of these 97 had a psychogenic cause (89 anxiety neurosis, 8 hysterical dissociation). Physiogenic conditions accounted for 11 (2 post-epileptic, 9 post-infective). The other 9 were cases of hysterical-malingering. The writer finds that post-epileptic automatism is the only condition in which the patient may be said

to be asleep. In all other cases the patients are awake, but with a varying degree and extent of awareness. Elaborate action would be evidence that almost the entire psyche is awake. It is concluded therefore that in the case of acts done during hysterical-malingering states a person may be held responsible. By the same argument it could be said that except perhaps for the katatonic stupor it is incorrect to say that the patients in a mental hospital are insane.

Lindner (1945) treated a man suffering from hysterical somnambulism by hypno-analysis. He concluded that in this case the basic phantasy was a triad of latent homo-sexuality, sadism and castration-anxiety. The somnambulant symptom was a protective mechanism used to escape the consequences of deeply entrenched id-urges and super-ego punitive demands. A further function was the avoidance of guilt.

Reviewing the literature on narcolepsy, Lehrman and Weiss (1943) estimate that nearly 700 cases have now been reported. Some regard the condition as a disease *per se*; others, including the writers, regard it as a syndrome that may accompany a number of pathological conditions. Though far from complete, Notkin and Jelliffe's classification is considered the most useful. This classification isolates 5 groups: (1) those with definite psychopathological background; (2) those with definite evidence of cerebral involvement; (3) those with chronic encephalitis; (4) cases with combined narcoleptic and epileptic attacks; (5) cases of the cryptogenic type. It is noted that only comparatively few with a psychopathological background have been reported (64 up to 1934), while the number in which the syndrome is associated with schizophrenia is still less.

These writers report on a woman with a schizoid personality who developed narcolepsy and cataplexy at the age of 15. She was at first very sensitive about her attacks, later definitely paranoid, and finally, aged 29, she was admitted to the mental hospital; diagnosis—schizophrenia, paranoid type. By this time the paranoid ideas were diffuse, and though the narcolepsy was controlled by benzedrine, the psychotic state was unaltered.

Discussing the causal relationship between narcolepsy and schizophrenia, it is observed that in cases of psychogenic origin, narcolepsy is seldom accompanied by cataplexy. It is concluded that in the present state of our knowledge this case should be classified in the cryptogenic group.

Furtado and Valente (1944) present a case of narcolepsy displaying the classical triad of the syndrome: in turn narcoleptic attacks, crises of cataplexy provoked by laughter and oneiric manifestations with very intense hallucinatory phenomena. The syndrome is regarded as the expression of a hyperexcitability and dissociation of the hypnic mechanism. Hyperexcitability is shown by disturbance of the normal sleep rhythm—the spontaneous narcoleptic attacks by day. That there is dissociation of the various elements constituting physiological sleep, dulling of consciousness, hypotonia and release of dreams is shown by the fact that in this disorder these elements appear in isolation as a narcoleptic attack, cataplectic crisis and oneiric manifestations.

The authors disagree with Wilson and others, who regard narcolepsy as essentially different from physiological sleep, approximating to coma, and affiliated with the epilepsies. Against this it is noted that in narcolepsy the

patient is easily roused and the clinical picture bears little resemblance to coma. Against a relation to epilepsy a number of points are made: The absence of hereditary constitutional factors; it does not lead to permanent psychic alterations; the absence of convulsive movements or of a qualitative disturbance of consciousness; the electro-encephalographic findings; and lastly the pharmacological findings (inefficacy of the anti-epileptics in narcolepsy; inaction or aggravation of symptoms of epilepsy by the adrenalin-like psychostimulants).

Like the epilepsies, it is convenient to divide the narcolepsies into two groups—essential and symptomatic. Causal factors of the symptomatic group are varied, and include epidemic encephalitis, cerebral tumours, cranial injuries, disseminated sclerosis. The site of the lesion is the infundibular region. The essential type may be due to a constitutional state or to infection, the aetiological factors remain unknown.

Cohn and Cravant's (1944) electro-encephalographic findings support the view that the narcoleptic syndrome is a member of the family of epilepsies.

Fabing (1945) describes the case of a soldier suffering from narcolepsy, cataplexy, and trance-like cataleptic attacks. He went through two campaigns and lived through many emotion-laden experiences. The fact that these attacks were a rare occurrence casts doubt on the view that cataplexy results from "emotional" stimuli, but that an excessively strong sudden stimulus causes a perversion of activity in cortical cells, so that a response destined to be excitatory becomes inhibitory. This is in accordance with Pavlov's theory.

Spiegel and Oberndorf (1946) present a case demonstrating psychogenic factors in a patient with narcolepsy. Catharsis, in the sense of disclosing memories both forgotten and voluntarily withheld, was effective in relieving the patient of her narcolepsy. It is concluded the psychogenic narcolepsy is a means of unconsciously satisfying forbidden wishes without experiencing guilt and simultaneously as a punishment for these wishes. The disappearance of the symptom induced a consciousness of guilt.

Millet and Mosse (1944) made a careful analysis of six patients. They concluded that narcolepsy is a personality reaction to emotional conflicts and not an organic disease. These patients are found to have in common a characteristic background of emotional conflict. They feel caught in a life pattern to which they are expected to conform, but which they deeply resent. They are frustrated in their efforts to achieve autonomy and self-differentiation, and in the tensions of the resulting emotional dilemma the narcoleptic symptoms appear.

Dynes (1943) has little to say about the pathology of this condition. He agrees with those who find a similarity between cataplexy and periodic familial paralysis. Administration of calcium chloride favourably affected the cataplexy, but had no effect on the narcolepsy.

Chodoff (1944) describes two cases of sleep paralysis. In both cases hypnogenic illusions were prominent, and in one precipitation of attacks by terrifying dreams occurred frequently. The symptom is recognized as a rare component of the narco-cataplectic syndrome. Both patients presented symptoms highly suggestive of this syndrome, nevertheless Chodoff does not think his cases can

be considered as typical narcolepsy unless the definition is unduly widened. Besides sleep paralysis, one case complained of attacks of sleep in the day which were not irresistible. He also complained that his knees gave way when he laughed, but that he did not fall. The second case complained of diurnal attacks of sleep of abrupt onset and when at work. The author concludes that sleep-paralysis is a non-diagnostic symptom occurring in true narcolepsy, in larval or incomplete narcolepsies (narcoleptoid states) and as an isolated phenomenon, appearing independent of any other disturbance of sleep motility functioning.

Heide and Weinberg (1945) present three cases of sleep paralysis in persons suffering from combat fatigue. The symptom occurred alone, and it is concluded that it is due to a state of confusion as to emotion and intention, with resulting indecisiveness.

Rudolf (1946) describes a condition known among nurses as "night-nurses' paralysis." It consists of a temporary tonic motor paralysis of insidious onset—consciousness is clear. It bears a strong resemblance to catalepsy, but whether its cause is psychological, chemical or neurological, or a combination of two or three, is not known.

SPEECH DISORDERS.

Meyer's investigation (1945) is based on a study of 116 cases. The frequency of families of stutterers is noted, but it is seldom possible to rule out imitation or other non-hereditary factors. Physical examination failed to reveal evidence of constitutional inferiority or organic disease in a significant number of cases.

Psychiatric investigation showed that the stutterer is often a schizoid individual. Many provided a history of bed-wetting, nail-biting and night-mares indicative of emotional tension. Analysis of the history of onset revealed in nearly 50 per cent. a specific aetiological factor—a fear situation. The subsequent history supports this, viz. close association between emotion and the speech disorder, capacity for stutter-free speech in favourable conditions.

It is concluded that stuttering is the resultant of a conscious wish to express oneself and an unconscious inhibition of speech. The latter appears to serve as a defence against anxiety. On these grounds the symptomatic "cure" of stuttering is condemned.

Despert (1943) notes that most personality investigations have been made on adult stutterers, in whom, therefore, secondary personality changes complicate the picture. In the author's series of 15 child stutterers a neurotic familial background was present in the majority of cases. More particularly it is found that the maternal neurotic attitude and oral orientation play an important role in the genesis of speech disorder. "The early eating-speaking situation can become traumatic if the child's rapport with the mother is being continually frustrated." In this connection it is noted that the onset of speech disorder in a majority of cases was between 2 and 3 years, "during a period when upper respiratory and upper digestive structures are gradually initiated into speech articulation." Further, this period is coincident with several critical developmental phases: change to solid food and self feeding, speaking,

walking, initiating of hand preference, and elimination control. The analysis also brings out the fact that there is a close relation between chewing and speech. Most writers have stressed the anal aggressive level of functioning as related to speech disorder. In this series 7 showed aggressiveness, while 8 were of the submissive type.

Usher (1944) reports an analysis of a boy of 6, in whom the stammering was intimately bound up with paranoid fears and anxieties along with accompanying secrecy and depression. Analysis, which resulted in normal speech and improvement in the mental symptoms, revealed that not only did the stammer serve the purpose of concealment, but, for the patient, "words-in-bits were the internal persecutors-in-bits being ejected."

Mass (1946) concludes that stuttering is a pure neurosis in rare cases only, but neurotic symptoms arise in the majority of stutterers later on. Stuttering is probably a congenital affection in some cases, perhaps the result of a brain injury during delivery. It usually starts in infancy, probably as a result of organic damage in the speech area or in speech centre association tracts. It is sometimes observed to start in adult life following a severe affection of the central nervous system.

Brody (1943) showed that permanent changes of the voice as well as alteration in voice production from time to time are reflections of emotional states, and are used by the ego as vectors for neurotic symptoms and defence mechanisms. It is found that the most difficult to influence are those arising from vigorous defensive processes in the past which have developed into permanent character traits.

SUICIDE.

Siewers and Davidoff (1943) made a comparative study in regard to 150 patients who attempted suicide prior to admission to a psychopathic hospital, and a similar group of 150 patients admitted to two general hospitals. At the psychopathic hospital patients with suicidal intent constituted 1 in 11 of the admissions, in the general hospital 1 in 370. Other points noted were: Psychoses predominated in the mental, psychoneuroses in the general hospitals. Patients with organic illness comprised a little less than one-third of all the cases in each group. Approximately three-fifths of the patients in each group were females. Sixty per cent. of those in the psychopathic hospital were over 40 years of age, 60 per cent. in the general were under 40. It was noted that in men of both groups self-destructive attempts were more common in later life. In women the psychotic group at the mental hospital most frequently belonged to the involutional period, while the psychoneurotic women in the general hospital were more prone to attempt suicide from 20 to 30. In regard to method employed, the general hospital patients inclined towards the use of phenol derivatives, iodine, illuminating gas, firearms, and incisions with sharp instruments. The mental hospital patients preferred to employ a combination of methods, and in general made more indecisive or indirect attempts. As regards motive, sexual maladjustment was given by about one-third of the patients of each group, economic difficulties in about 15 per cent. of each group.

TELEPATHY.

Fodor (1947) reports five dreams, which were shared among two or more of four persons, including the writer. It is suggested that the circumstances are such as to rule out coincidence as more fantastic than the recognition of some unknown mechanism. It is concluded that telepathy is a mechanism operating wholly or predominantly on the unconscious level, possibly due to a special cognitive faculty of the unconscious. It is also suggested that, since this dream series occurred among persons with strong emotional ties, such ties may be pre-requisite for telepathic dreaming.

Eisenbad (1946-47) describes his experiences of telepathy in the psychoanalytic situation, including a "*rêve à deux*" by individuals unknown to each other. Pederson-Krag (1947) also cites examples of telepathic dreams.

For Ehrenwald (1948) there is statistical evidence to make telepathic phenomena an established fact. His evidence is based on a study of telepathy in dreams, the psychoanalytic situation, mediumistic trance, paranoia and schizophrenic deterioration. He concludes that the conscious ego is bombarded with hetero-psychic as well as auto-psychic stimuli. In man's attempt to achieve a self-contained psychological entity from the rest of the world, hetero-psychic influences have been repressed and denied. The medium, however, trains himself to yield to them, the paranoiac struggles against them, while in schizophrenics the massive intrusion of these experiences leads to final disintegration of the personality.

Ehrenwald's attitude towards telepathy would appear to have been determined by an experience when a medical student. A fellow student developed paranoid schizophrenia and came to regard Ehrenwald as one of his chief persecutors. The latter detected in himself ambivalent feelings towards the psychotic, and believed he had become aware of them by hetero-psychic influence. The fact that Ehrenwald had consulted Professor Pick about his friend and that this had led to his admission to a mental hospital would appear a sufficient motivation for hostility.

In a critique of recent telepathic "findings" by Eisenbud, Pederson-Krag, and Fodor, Ellis (1947) concludes that they rest on flimsy evidence. He points out that the investigators were all convinced of the existence of telepathic phenomena. They all interpreted the term telepathy very loosely, and found "telepathic evidence where one event occurred simultaneously with, prior or subsequently to a supposedly congruent occurrence." They all preferred to accept coincidental and chance dual occurrences as unmistakably "telepathic" ones. They all interpreted normal analytic occurrences so as to fit in with preconceived telepathic notions. They conveniently linked material that was manifest or latent, conscious or unconscious, symbolic or non-symbolic, interpretative or non-interpretative, whenever and wherever such material could possibly be made to fit into a telepathic hypothesis. They all presented "telepathic" dreams relating to patients who were closely involved with them, and who often were convinced of the occurrence of telepathy. They also presented dream sequences whose content and associative material could have been easily suggested to the patient by the reporting analyst. They all tended to capitalize on the laws of chance by continually looking for "telepathic"

dreams in all their patients. In conclusion he summarizes the criteria he regards as essential for the substantiation of telepathic dream phenomena.

TICS.

Mahler (1944) thinks that tics can be tentatively classified into three types. First there are tics resulting from a conflict between an overtaxed affective motility and the claim for control. They start very early in life, and are characterized by great interchangeability of the movements involved. At first they can be voluntarily controlled, but by the age of 6 their volitional character is lost. In the second type the tic starts at school age, but there is often a pre-school history of fidgetiness. The tic, often associated with general jerkiness, appears a few weeks after the child has given up auto-erotic activities. In contrast to the first group this type is very inhibited in its voluntary expression. The third type appear first in adolescence and adults. These tics seem to have a more localized affinity to the eroticized organ, for which the tic muscle group is used as a symbolization. Their psychodynamics are like that of traumatic neuroses.

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NEUROPATHOLOGY IN RELATION TO MENTAL DISEASE.

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INTRODUCTION.

This review differs from the previous one (Meyer, 1944) in that it is still more strictly confined to neuropathological problems of interest to the psychiatrist. The Section on the Pathology of Oligophrenia has been taken over by Dr. R. M. Norman. On the other hand, there is a much wider field to review since the continental literature has become once more available. A certain overlapping with other chapters, particularly those on physiology and biochemistry, is inevitable if one is not to deprive pathology of much of its function as an instrument of integration.

GENERAL DEVELOPMENTS AND NEW TECHNIQUES.

The technical revolution being caused by rapid advances in biophysics and biochemistry continues to have its repercussion on neuropathology, and although it is too early yet to expect concrete results in the field of the pathology of mental disease, these are bound to come. It seems, therefore, proper to start this review with a brief outline of some of these new lines of research.

In the *anatomical* field specialized silver techniques have been used to trace degenerating fibre tracts. The advantage of this method over other techniques, such as the Weigert-Pal and Marchi methods, is that it permits the demonstration of the actual axis-cylinders, particularly their terminal arborisations, thus showing up the nerve fibre irrespective of its degree of myelination. The technique is notoriously difficult, but in the hands of experienced workers has already yielded important results, such as the demonstration of degenerating terminals within the caudate nucleus after ablation of the suppressor area 4s in the cat (Glees, 1944) and the tracing of olfactory connections by Le Gros Clark and Meyer (1947) in the rabbit. Again, with the same method Meyer (1949) has demonstrated, in material from leucotomized patients with short

survival period, a direct fibre connection from the dorsal frontal convexity (approximately areas 8 and 6 of Brodmann) to the mammillary body and other parts of the posterior hypothalamus.

Interest in methylene blue as a vital stain for the demonstration of nerve fibres, and in particular of degenerating fibres and terminals, has been renewed recently in a series of interesting studies coming from the Department of Human Anatomy in Oxford (Feindel, Sinclair and Weddell, 1947; Feindel, Allison and Weddell, 1948). It is used in a similar way to the silver technique. The two may be usefully combined, but in virtue of its being a vital stain, methylene blue is largely confined to experimental animal work.

Techniques and investigations of this kind are of interest to the psychiatrist because they are bound to play a large role in the process, so far barely begun, of disentangling the structural complexities of the brain. The introduction of neurosurgical operations for the treatment of mental patients has served as a powerful stimulus to research in this direction. The gulf between anatomy and physiology is rapidly disappearing. Anatomy is no longer the descriptive science of the past, but has largely become experimental in the hands of its foremost contemporary exponents, such as Ranson, Le Gros Clark, Walker, Mettler, von Bonin and others, whilst the neurophysiologists have become distinctly anatomically minded. In the hands of Dusser de Barenne and McCulloch and their collaborators, the anatomical exploration of the living brain by means of strychnine stimulation and oscillographic recordings (physiological neuronography) has led to an astonishing revival of interest in anatomical research and to far-reaching results, of which the discoveries of the so-called suppressor bands in the cerebral cortex and facilitatory and inhibitory centres in the brain-stem and cerebellum are perhaps the most important to date, since it has revolutionized concepts of extrapyramidal function. Other far-reaching results achieved mainly by oscillographic methods are the discovery of a second motor and sensory cortex within the parietal operculum, the establishment of fronto-hypothalamic connections, the demonstration of autonomic function in the posterior orbital region and the cingular region, and the gradual elucidation of obscure pathways such as the short and long association tracts. This is not the place to review these results in detail; those interested are referred to reviews by McCulloch (1944), McCulloch and Lettvin (1948) and Fulton (1949). These oscillographic findings have greatly stimulated histological corroborative research. Mention has already been made of Glees' observations on cortico-striatal connections and Meyer's histological confirmation of fronto-hypothalamic connections.

The deepening penetration of *electronic principles* into neurophysiology has led to radically new concepts of brain function. These have found their most complete expression so far in the book on *Cybernetics* by Wiener (1948), the constructor of one of the great electronic computing machines. In a historical chapter Wiener gives an outline of the developments which led up to the introduction into neurophysiology of well known electronic concepts, such as reverberating circuits, negative feed-back, scansion and oscillation. (See also the reviews of the book by Cobb, 1949; Ashby, 1949, and Brazier, 1950.) The essence of reverberating circuits is that a closed chain of neurones can be

set in action by a single incoming impulse, and the impulse continues to pass round the circuit as long as metabolism supports it or until other incoming impulses change it. Feed-back implies a mechanism by which the activity of a dynamic system is modified by the return of some fraction of the output of the system as input; in a servo-mechanism the feed-back is so arranged that it maintains the whole system in a state of dynamic equilibrium; in a homeostat this arrangement is found automatically by the machine itself. Scansion is a term derived from television and means a rhythmic sweep of impulses in non-specific afferents (perpendicularly or otherwise) through the cortex. It has been suggested that the alpha rhythm is the "smoke" of this rhythmic sweep, energized perhaps, from the thalamus. Oscillation is a common phenomenon in servo-mechanisms, due to faulty feed-back. Simple excessive negative feed-back can produce excessive stability, i.e. rigidity or fixity, rather than oscillation.

Not only has extrapyramidal function and dysfunction been given a new explanation, but, what is more important to psychiatrists, a physiological interpretation has been suggested for psychological processes, such as perception of universals, memory and purpose. It is beyond our terms of reference to discuss the psychological and philosophical implications of these new concepts; this, it is hoped, will be done elsewhere in the present volume by more competent reviewers. These new ideas have been hailed, on the one side, as removing once and for all any need for dualistic interpretation of the mind-body problem (Northrop, 1948) and as offering concrete solutions to the problems of mental function and disease. On the other extreme, they have been rejected as incapable of ever explaining humanistic values (Jefferson, 1949). The present situation is, to some extent, reminiscent of the period which followed the promulgation of the theory of evolution; over-optimism on the one side and indignant reaction on the other; neither exclusively right in the light of subsequent history. It would be futile to resist the application of advances in the fundamental sciences, but about equally futile to expect them to furnish short cuts to the solution of all biological mysteries.

The analysis of microscopic structures in the light of these new mechanistic concepts has hardly begun. Pitts and McCulloch (1947) have carried out an analysis of the auditory and visual cortex in the light of the successful construction of a reading machine for the blind, utilizing electronic scanning circuits. It is reported by Wiener that when the diagrams for the wiring of the photo-electric cells were shown to von Bonin they immediately suggested to him the fourth layer of the visual cortex. This is, indeed, a fascinating and novel way of looking at cortical architecture.

There have been considerable developments in *biochemistry* in relation to the central nervous system, which will be reviewed elsewhere in this volume. A much clearer picture can now be given of the main energy-yielding reactions in the brain (McIlwain, in press), and of changes in chemical constituents with varying activity of the central nervous system. The determination of cerebral metabolism by arterial-venous difference has now reached a high level of accuracy (Gibbs, Maxwell and Gibbs, 1947) and variations in such metabolism under different physiological and pathological conditions have been studied.

The first reports have appeared of well-controlled metabolic investigations with slices of human brain tissue from neurosurgical operations (Elliot, 1948.)

A greater critical sense is now appearing in the application of clinical chemistry to neuropathological and psychiatric conditions. A note of caution against a too ready application of findings in clinical chemistry was sounded in the review of Folch (1947), as well as in the discussion at the Royal Society of Medicine (1945), in which Greville, Richter, Quastel and Benesch took part. Greville suggested that changes in glucose tolerance in melancholia and in hippuric acid synthesis in catatonia are secondary phenomena. Investigations regarding glutamic acid (Albert, Hoch, Waelsch, 1946), and carbonic anhydrase (Ashby, 1947) in relation to mental function and dysfunction must also be regarded as in their experimental stages.

Various advances in *histochemistry*, ably reviewed by Dempsey and Wislocki (1946) and by Glick (1949), are of special interest from the neuropathological angle. They are too many to be enumerated here, but research on the histochemistry of nucleotides, alkaline and acid phosphatases and lipases should, perhaps, receive special mention. Acid phosphatase, which disappears in degenerating neurones, has been used as a histochemical test of degeneration (Hard and Lassek, 1946). Special mention should also be made of a systematic attempt by Feldberg and Vogt (1948) to study the distribution of acetylcholine synthesis in the central nervous system. They found interesting differences between upper and lower motor neurones, and between motor and sensory neurones.

The various new *microscopic techniques* continue to arouse much interest, reflected in a recent annotation in the *Lancet* (1948), although their application to the central nervous system is still in an embryological phase. Barer (1947) and Zollinger (1948*a, b*) have made cytological studies with the phase contrast microscope, the former stressing the advantages of this method for the demonstration of nerve cells in particular. Striking results are reported by the use of ultraviolet microscopy. Caspersson and his collaborators in Sweden have developed this as a new branch of cytology which they have named "microspectrophotometry" (Caspersson and Santesson, 1942; Hyden, 1947; Caspersson, 1948). The highly specific absorption of Nissl bodies at about 2,600 Å. indicates that a high concentration of nucleic acid occurs in the Nissl bodies (thus confirming views held by older neuro-anatomists). The technique has been applied to the study of cell growth and reproduction and certain other physiological as well as pathological conditions, such as chromatolysis in fatigue and after sensory stimulation, retrograde degeneration and cytology of carcinoma cells. Hyden and Hartelius (1948) found, in biopsy specimens taken out during frontal leucotomy performed on schizophrenics, a lack of nucleotides in the nerve cells as compared with control material. However, certain fallacies in the interpretation of nerve cell degeneration in biopsies have to be taken into account, as has been pointed out by Meyer and Meyer (1949). The realization of these fallacies is of some practical importance, since the observations of the Swedish authors form the rationale of the treatment of mental disease with malononitrile.

The reflecting microscope, designed by Burch (1948) and now built also in the United States (Seeds and Wilkins, 1949) also depends on the properties of the ultraviolet rays. It dispenses with optical lenses, which tend to cut out this range of the spectrum, replacing them by suitably arranged mirrors. The observations on nerve tissue obtained with this microscope have so far been published.

The chief obstacle to the application of electron microscopy to the investigation of biological specimens is still the necessity of drying specimens and exposing them to a vacuum (see the review by Coslett, 1947). This obstacle is now in process of being overcome by the use of a capsule (Abrams and McBain, 1944) and the introduction of high-speed microtomes (O'Brien and McKinley, 1943; Fullam and Gessler, 1946; Newman *et al.*, 1949) which are claimed to cut uniform sections of 0.1 to 1.0 μ in thickness. It is due to these technical difficulties that the pace of advance achieved by the electron microscope so far has been greatest with material which can be observed in dried films, for instance, viruses and muscle fibres. On the latter much interesting work, particularly on the physico-chemical basis of contraction, has been done recently (e.g. Reed and Rudall, 1948; Snellman and Erdös, 1948; Astbury, Reed and Spark, 1948; Perry, Reed, Astbury and Spark, 1948). These studies are mentioned because once before decisive advance in the elucidation of muscle physiology preceded that of nerve physiology. In the latter field, however, contributions, so far, are only scanty (e.g. Robertis and Schnitt, 1948; Callan, Randall and Tomlin, 1949), but once the technical problems are solved an immense field for research of the greatest importance will be thrown wide open.

Like electron microscopy, X-ray diffraction photography has not yet been widely applied to the study of the central nervous system. In Spiegel-Adolf and Henny's monograph (1947), which reviewed work in biology and medicine, only investigations of a preliminary character on peripheral nerves were mentioned. Most electron diffraction work in the future will probably be done with adapted electron microscopes, and not in special diffraction cameras. Such combined instruments are already being commercially manufactured in Britain (Coslett).

Finally, there remains to be mentioned the method of *autoradiography*, which permits of tracing radioactive isotopes in relation to histological sections. One section is "photographed" by contact with an electro-sensitive emulsion and the tracings in this emulsion are then compared with, or superimposed on, an adjacent section stained by orthodox neurohistological methods. This method was introduced by Belanger and Leblond (1946), and more recently has been developed by Boyd and Williams (1948). To our knowledge, no work so far has been done on nervous tissue, the thyroid gland having been the main focus of attention. Nor has there so far been any appreciable volume of work on problems of the nervous system by means of the ordinary tracer, geiger-counter, technique. Both of these methods would seem likely to hold great potentialities for the elucidation of problems such as, for instance, those of selective vulnerability, the blood-brain barrier, and the site of action of drugs.

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INFLAMMATORY DISEASES.

The greatest advance in this group of diseases has been in the field of the *Virus Infections*, a fact of very considerable practical interest to the psychiatrist, for experience of recent years shows that he encounters cases of encephalitis among his patients, especially children, more frequently than is generally realized.

The day of visual identification of at least some pathogenic viruses would seem to be near. Electron microscopy has already shown not only some structural differences between the elementary bodies in the vesicle fluid obtained from variola or vaccinia and that obtained from varicella (Nagler and Rake, 1948), but also discrete entities, for instance, which may be the actual viruses of influenza (Chu, Dawson and Elford, 1949) and of poliomyelitis (Gollan and Martin, 1948), the smallest living organism known to infect man.

The older, rough, clinico-pathological grouping of the virus infections of the central nervous system begins to be reinforced by reliable aetiological classification by means of isolation of the viruses through animal passage and their identification in terms of specific antigenic reaction. The usual method of isolation involves the intracerebral inoculation into animals of blood or cerebrospinal fluid taken from the patient. In the case of viruses which cannot be so isolated, other immunological methods are employed, such as neutralization tests of the patient's serum against known viruses, and complement fixation tests. The present position has been stated by Rhodes (1948) and reviewed by Gear (1949), who both utilize the antigenic reaction of the causative virus as well as the anatomical incidence of the pathological lesions and the known vectors, to classify the neurotropic virus infections of man. Both the clinico-pathological and the antigenic (Hammon, 1948) resemblances within the group of arthropod-borne encephalitides (i.e. the mosquito-borne St. Louis, Japanese B, West Nile and various equine types; and the tick-borne louping-ill and Russian spring-summer encephalitides), suggest that the whole group of viruses responsible may be interrelated and derived from a common stem virus.

The natural history of *poliomyelitis* has been reviewed by Lacey (1949). Transmission of the disease is now widely held to be largely through faeces, and less definitely through the agency of flies, whilst the consensus of opinion now appears to be that the virus does not gain entrance to the human central nervous system by way of the olfactory nerves, but probably by the nerves of the throat and gut. Multiplication has been shown by several workers to be almost restricted to certain cells, namely, the motor neurones of the anterior and lateral horns, the reticular formation of the brain stem, the vestibular nuclei and the roof nuclei of the cerebellum. Bodian (1948*b*, 1949) attributes the selectivity of the lesions to "specific differences of susceptibility of nerve cells and to nerve fibre connections," i.e. pathways along which viruses move. He found the pontine nuclei and inferior olives to be notably spared and lesions in the motor areas of the cerebral cortex to be rarely severe enough to suggest responsibility for production of clinical symptoms. Thiamine deficient animals are more resistant to the virus (Gear), whilst desoxypyridoxine (antivitamin) treatment makes them more susceptible (Bodian, 1948*a*). Russell (1947, 1949) has deduced that fatigue and violent exercise predispose an infected individual to paralytic attack. There is as yet no routine laboratory diagnostic test short of intracerebral inoculation of monkeys. It has recently been demonstrated (see Gard, 1949) that poliomyelitis is a symptom complex produced by at least three antigenically distinct groups of viruses.

So-called *post-infective encephalitis* (dengue, herpes febrilis, herpes zoster,

infective hepatitis, influenza, lympho-granuloma inguinale, measles, mumps, rubella, sandfly fever, variola and varicella; and the post-vaccinal encephalitis of smallpox and yellow fever) is now widely held to be a manifestation of allergy. According to Gear, "experiments carried out by Kabat, Wolf and Seizer (1947) and Morgan (1947) support the hypothesis that post-infective and post-vaccinal encephalomyelitis may be regarded as auto-allergic or auto-antigen-antibody reactions to some component of the central nervous system tissue made auto-antigenic by the presence of virus. The neuro-paralytic accidents following anti-rabies vaccination may similarly be regarded as reactions due to the development of antibodies to this component, following the injections of nervous tissue. In these experiments a picture resembling acute disseminated encephalomyelitis in the human being was produced regularly and rapidly in rhesus monkeys by injections of emulsions of homologous monkey brain administered with an adjuvant, paraffin oil, in which heat-killed dried tubercle bacilli were suspended. Morgan noted that positive reactions occurred only in response to central nervous system tissue containing white matter. An analysis of the results suggests that the antigen concerned is the myelin of the white matter of the central nervous system."

Gear concludes his review by speculating as to whether a number of other obscure conditions of the central nervous system—like disseminated sclerosis, many drug encephalopathies, amyotrophic lateral sclerosis, Schilder's disease, and others—may not be manifestations of similar auto-antigen-antibody or auto-allergic reactions. A newly described acute necrotizing encephalitis is thought by Adams, Cammermeyer and Denny-Brown (1949) to be probably allergic in origin.

Cases of *subacute encephalitis* have drawn much attention during the period under review. Van Bogaert (1945) described three Belgian cases of a clinicopathologically distinctive type which he called "subacute sclerosing leuco-encephalitis" in virtue of the widespread glial fibrosis in the white matter with little or no demyelination. Dellaert, Maere and van Bogaert (1945) almost immediately identified another. Rosanoff (1947), working in our laboratory, found a very similar clinical and histological picture in the case of an English girl, aged 6, and two more such cases have since been studied in our laboratory, one of them having a somewhat shorter course and more marked demyelination than any of van Bogaert's cases. The common clinical features comprise insidious onset in childhood with liability to aphasia and apraxia, and a subacute course with gradual development of extra-pyramidal spasticity, involuntary jerking movements, decerebrate rigidity and cachexia, over a period of six to twelve months. The electroencephalogram shows episodic, and later periodic, bursts of slow wave activity, terminating at the moment of the involuntary movement (Cobb and Hill, in press). Rosanoff at the same time described two other subacute cases, one of which he considered resembled one of Noran and Baker's (1944) chronic cases of Western equine encephalitis. Noran and Baker (1945) demonstrated that Western equine encephalitis may occur in a subacute as well as chronic form. These authors conclude that the virus of this type of encephalitis primarily attacks the blood vessels and may remain active for many years. Another important subacute type is the inclusion-

body encephalitis called after Dawson. This condition has been reviewed with the addition of two new cases by Brain, Greenfield and Russell (1948). A feature of some importance to psychiatrists is that several of these cases of subacute encephalitis were admitted directly to a mental hospital on account of the early manifestation of mental symptoms.

Finally, brief mention should be made of reports of three human cases of herpes simplex encephalitis (Haymaker, 1949); of two fatal cases of infectious mononucleosis resembling poliomyelitis (Ricker, *et al.*, 1947); of naturally acquired human infection with louping-ill (Davison *et al.*, 1948; Brewis *et al.*, 1949); and of Hassin's (1945) toxi-productive form of encephalitis which he considers to be more common in children and adults than any other form of encephalitis.

As regards *Non-Virus Infections* the publications of most interest to the psychiatrist are probably those concerned with chemotherapy and those dealing with some peculiarly war-time neuro-psychiatric problems.

The only description so far of the histopathological findings in cases of death occurring shortly after treatment of *Dementia Paralytica* with penicillin has been by Smith and Morais (1948), working in our laboratory. They found that in two patients who had improved clinically as well as serologically, but had died of intercurrent illness, the brain showed inflammatory changes and iron reaction distinctly less intense than in the average untreated general paretic and very similar to the findings at comparable times (6-15 weeks) after start of treatment with malaria. Their other two cases were of the juvenile type of G.P.I., had deteriorated rapidly during and after penicillin therapy, and showed no mitigation of the inflammatory or iron reaction. They concluded that penicillin alone is capable of influencing the pathological progress of general paresis. Two more recent cases investigated in our laboratory (but not published) confirm this conclusion.

Zollinger (1948) has described the pathological findings in 22 cases of *Tuberculous Meningitis* treated by streptomycin. There was evidence of considerable healing (of no special type) of the tuberculous lesions, leaving arachnoidal scars. He and his associates considered that much of the clinical failure was due to vascular lesions and that, therefore, to be effective streptomycin treatment must be started before diffuse exudation and vascular lesions are established. When caseation had taken place there was a danger of exacerbation, in the form of renewed subarachnoid spread, being aroused by the treatment. Daniel (1949) likewise emphasized the importance of early treatment to minimize the formation of exudate within the basal cisterns—an exudate which, as the result of streptomycin treatment, becomes tough and woody and liable to cause obliterating arteritis at the origins of all the major cerebral arteries, and hydrocephalus (De, 1949).

The recent war was largely responsible for many fresh observations on the neuro-psychiatric manifestations during the course of *Malaria*, by workers such as Arieti (1946), Irish (1946) and Boshes (1947). It is generally agreed that the most, though not exclusively, responsible organism is *Plasmodium falciparum*. Although Rigdon and Fletcher (1945), in describing their experimental studies on various animals, placed main emphasis on the general anoxia resulting

From the anaemia and myocardial affection, the pathogenic mechanism is generally accepted to entail, in addition, a diffuse occlusion of small cerebral vessels probably by parasitized red blood corpuscles causing foci of necrosis and petechial haemorrhages. The histological changes are considered to be at times the direct cause of, and at other times only precipitating factors in, the mental syndromes, which may take almost any form.

Overseas military campaigns likewise determined the appearance of several papers on *Schistosomiasis* affecting the brain. Kane and Most (1948) reviewed the clinical literature, added 24 new cases and described oedema, necrosis, infiltration and ova in the brains of five which came to autopsy. Chang and his associates (1948) described a similar histopathology in four cases; Hunt and his co-workers (1948) in one more. No special psychiatric syndrome peculiar to the infection is described by any of these authors.

The lesions in the central nervous system in *Scrub Typhus* (*Tsutsugamushi fever*) were considered to have no site of predilection by Ripley (1946), who found the lesions to consist, as elsewhere in the body, of focal thromboses and necroses with perivascular infiltration by lymphocytes and plasma cells. Mental symptoms were conspicuous and apparently influenced "as in other toxic conditions by the personality, background and emotional reactions of the patient." Weil and Haymaker (1946), on the other hand, found the lesions in a detailed study of 21 cases to favour periventricular regions, the basal ganglia and the amygdaloid-hippocampal complex.

Colover (1948) has surveyed 118 cases of *Sarcoidosis* with involvement of the nervous system. He concluded that the structures most liable to be affected are the optic nerves and retinae, the 7th, 9th and 10th cranial nerves, pars intermedia of the pituitary gland, the pituitary stalk and the peripheral nerves. Many observers hold the view that the disease is an atypical form of tuberculosis. Green (1943) described a case of chronic tuberculous meningo-encephalitis simulating a tumour of the hypothalamus and showing many histological features resembling sarcoidosis.

Two cases of infection of the central nervous system by *Torula histolytica* simulating cerebral tumour were described by Swanson and Smith (1944), and another by Krainer and his associates (1946); one simulating tuberculous meningitis by Magarey and Denton (1948); and two simulating tuberculous meningitis by Daniel, Schiller and Vollum (1949).

Toxoplasmic Encephalitis in a new-born child was fully described and illustrated by Steiner and Kaump (1944). This was the fifteenth case reported in the literature since 1937. The first case diagnosed clinically in this country was described by Jacoby and Sagorin in 1948, but there has been no report of autopsy on any case in the United Kingdom, beyond a dog referred to by these authors. Frenkel (1949) has published an excellent review of the pathogenesis, diagnosis and treatment of human toxoplasmosis.

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VASCULAR DISEASES.

No major advance regarding the pathogenesis of *Arteriosclerosis* has been recorded in the past five years, with the exception perhaps of Wilens' (1948) observations on orthostatic influences on the distribution of atheromatous lesions in the cerebral vessels in relation to the length of the neck and other aspects of body configuration. Mention should be made also of Leary's (1949) demonstration that atherosclerotic lesions are due to crystalline esterification of excess cholesterol in the Kupfer cells of the liver, whence it is transported by the blood and deposited in the subendothelial layer of the arterial intima in regions where cholesterophages can contact the intima. Alpers, Forster and Herbut (1948), from a study of material from 100 human adults, were not able to demonstrate any consistent correlation between retinal and cerebral

arteriosclerosis. Recent work on the relationship of arteriosclerosis to physiological ageing is discussed in the Section on Ageing.

Äring (1945) and Scheinker (1943, 1945*b*, 1948*a*, 1948*b*) have pressed strongly their concept, obviously derived from the much earlier work of Ricker and Spielmeyer, of the essential role played by functional abnormality of the cerebral blood vessels, i.e. excessive range or lability of vasomotor control, in such conditions as migraine, thrombo-angitis obliterans, embolism, hypertensive softening and cerebral haemorrhage (as well as disseminated sclerosis). In vasostasis and vasoparalysis of veins and venules they see, for instance, the origin of the haemorrhage in arteriosclerotic and hypertensive apoplexy. In cerebral thrombosis they have never been able to detect thrombi, in cerebral haemorrhage aneurysm or perivascular softening; from reversible stasis with congestion the venous pathology goes on to atrophy and advanced degeneration of the vessel wall, giving rise to diapedetic petechiae and larger haemorrhages. This concept of vasoparalysis was invoked again in interpreting the autopsy findings in a case of toxic encephalopathy caused by streptomycin therapy of a patient with restricted renal function (Hunnicut, *et al.*, 1948).

In the brain of a schizophrenic patient who developed sudden hemiplegia during an acute catatonic episode, Murphy and Neumann (1943) described gross haemorrhagic lesions which they attributed to "the functional circulatory changes often associated with the form of mental illness." They considered that the case tended to substantiate von Braunmühl and Spielmeyer's theory that functional circulatory disturbances operate as an important factor in acute catatonic excitement. They briefly review the literature on anatomical studies in catatonia.

Thrombosis of large cerebral veins and sinuses has been reviewed by Martin and his associates (1944), and discussed in eleven cases by Perrier (1947/8) in the light of Symond's original description of the condition and of the paravertebral system of venous anastomoses. Perrier considers that the prognosis is often favourable, the vessels recanalizing. Kendall (1948) favours the view that puerperal cerebral thrombosis is primary rather than due to retrograde venous embolism from the pelvis via vertebral veins.

Alexander and Woodhall (1943) have postulated that calcified lesions (such as found in epileptogenic foci, Sturge-Weber's disease, tuberosclerosis, toxoplasmic encephalitis and oligodendrogliomata) are caused by incomplete interference with the capillary irrigation of a necrotic area. Strassmann (1949) has reviewed the time factors in appearance of haemosiderin and haematoidin after cerebral haemorrhages.

During the five years under review, *Allergy* as an aetiological concept has received much more general acceptance in this country than hitherto, though how the immunological reaction injures the tissues in which it occurs is still obscure. Rackemann (1948) is convinced that antigen-antibody reactions releasing H substances is the "heart and soul of the allergy," whether or not the same release can be precipitated by other mechanisms, such as infection, intoxication and depletion. Some mention of the role of allergy in the causation of post-infective encephalitis has already been made in the preceding section.

The vascular conditions which are widely thought to be allergic and which may occasionally result in mental symptoms as well as central neurological symptoms, are periarteritis nodosa, temporal arteritis and rheumatic endarteritis. Thromboangitis obliterans is usually classed along with this group of conditions—all of which have been receiving a growing amount of attention.

A well balanced review of clinical aspects of *Periarteritis Nodosa* has been published by Miller and Daley (1946). They favour the view that the condition represents a non-specific hypersensitive reaction of anaphylactic type to a variety of antigens, and consider that there is much evidence that the changes in the blood vessels differ only in degree from the less severe acute arteritis seen in acute rheumatism. These changes Miller (1949) conceives of as due to the repeated whealing of chronic recurrent urticaria of the blood vessels leading ultimately to multiple focal necrosis of their walls.

Involvement of the central nervous system, previously variously estimated to have occurred in from 8 per cent. to 20 per cent. of cases in the literature, was found early in the symptomatology in 7 of 16 fatal cases investigated by Parker and Kernohan (1949). Two had been diagnosed as cases of multiple cerebral abscess, one as a rapidly growing glioma and a fourth as a case of cerebral arteriosclerosis. Chronic polyneuritis was the predominant feature in the three others. Lovshin and Kernohan (1949) emphasized the frequency of peripheral neuritis in the condition and the importance of considering it in the differential diagnosis of any obscure disease with development of polyneuritis. In all 15 cases with neuritis the degeneration of nerve bundles proved to be due to closure or narrowing of the nutrient arteries (*vasa nervorum*).

Numerous reports of isolated cases have reinforced belief in the allergic origin of the condition, for example, its appearance after exhibition of arsenical drugs (Miller and Nelson, 1945; Turner and Paterson, 1946), sulpha drugs (Rosenak and Maschmeyer, 1945; Black-Schaffer, 1945), thiourea (Gibson and Quinlain, 1945), iodine (Rich, 1945) and diphenylhydantoin sodium (Wyk and Hoffmann, 1948); and after scarlatina (Peale *et al.*, 1946).

Rich and Gregory (1943) and Ralston and Krale (1949) assumed the concomitant glomerulonephritis in experimental and human periarteritis nodosa to be another consequence of the hypersensitivity. Zeek, Smith and Weeter (1948), on the other hand, distinguished between the histological features of periarteritis nodosa and of hypersensitivity angitis and offered experimental evidence (Zeek and Smith, 1947) to prove that the former may be caused by sharply rising hypertension irrespective of any anaphylactic process. They attribute Rich and Gregory's experimental findings to the concomitant acute glomerulonephritis. Selye (1946) and Timiras and his associates (1949) have produced lesions closely resembling periarteritis nodosa by administering desoxycorticosterone in large doses.

Cooke and his associates (1946), in reviewing 31 cases of *Temporal Arteritis* in the literature and 7 new cases of their own, discuss clinical as well as pathological points of difference, especially from cerebral periarteritis nodosa and cerebral thromboangitis obliterans. They conclude that "there exists in elderly people a widespread arterial disease, not uncommon but rarely recognized, in which characteristic arterial and striking local signs occur, and in

which inflammatory and degenerative changes in the walls of the affected arteries produce a characteristic histological picture." A more recent review by Crosby and Wadsworth (1948) deals with 43 cases in the literature and 5 additional ones. They agree in large measure with the foregoing authors, likewise stress that blindness is relatively common, and deduce that the systemic symptoms probably indicate a more generalized arteritis, since in the four cases with fully recorded autopsy, vascular lesions similar to those in the temporal artery were found in other vessels of the body. The main histopathological feature is a granulomatous type of reaction in the media. Multinuclear giant cells form a conspicuous component of the lesions, and "although not pathognomonic of this disease, are usually distinctive." They conclude that while temporal arteritis probably represents a much more widespread vascular disease than the name indicates, the inflammation of the temporal arteries has thus far remained the constant and dominant feature of the disease. Miller (1949), on the other hand, considers the essential differences from periarteritis nodosa to be clinical rather than pathological, stressing especially the lateness of onset and the invariably favourable prognosis. Gordon and Thurber (1946) argue that temporal arteritis represents periarteritis nodosa in an older age group. Harrison (1948), after reviewing 75 cases in the literature, rejects this view. That it is not just a localized variant of periarteritis nodosa would seem further evidenced by the demonstration that performance of biopsy (Myers and Lord, 1948; Kaye, 1949), or blockage of the sympathetic nerve fibres (Roberts and Askey, 1948), on the affected vessels, cures the symptoms and causes the vessels to relax and become soft. These facts would indicate the condition to be due to acute vaso-spasticity rather than primary arterial degeneration. This might remove it from the realm of allergic diseases.

Thromboangitis Obliterans affecting the brain has been reviewed by Davis and Perret (1946/7). In describing 11 new cases with symptoms and signs similar to those produced by a slowly growing intracranial tumour, they discuss the clinical syndrome in general and the diagnostic value of air encephalography in particular. Craniotomy and biopsy were performed in 9. Eight proved to be purely cerebral. Granular atrophy of the cortex was a constant finding. In a briefer review, Perk (1947) listed the few histopathological studies of the brain in thromboangitis obliterans and noted that mental symptoms are less frequent than neurological ones, ranging from transient confusion or excitement to full-fledged psychosis (of no specific type). Change of behaviour was the first abnormality noted in his personal case. He conceived of two mechanisms at work—a slow progressive occlusion of vessels and a superimposed paroxysmal spasm.

The first lesion in thromboangitis obliterans is conceived by Scheinker (1945a) to comprise small intramural haemorrhages, these in turn being due to prolonged vaso-spasm. The aetiology of the vaso-spasm has not been elucidated. Other aspects of thromboangitis obliterans have been mentioned by Llaverro (1946), Morel (1947), Minkowski (1947/8), Carrara (1948) and Meyer (1948).

Interest in *Rheumatic Arteritis* has been revived by Bruetsch's (1947) claim to have found rheumatic endarteritis within the brain, together with evidence

of old rheumatic heart disease, in 5 per cent. of the patients of a general mental hospital. The condition, which involved most frequently the small vessels of meninges and cortex, resulted in microscopic areas of softening in the cortex and a mental disturbance depending on age and previous personality. He concluded that in childhood aberrations may range from mild behaviour disorders to slight mental deficiency; in young adults a psychopathic picture suggesting schizophrenia may result. In middle life, and even in the aged, the end result may be a psychosis. Reviewing mental hospital autopsy cases from the clinical diagnostic angle he found the highest incidence (9 per cent.) of rheumatic pathology of the heart to be in patients with schizophrenia and concluded that rheumatic brain disease may well be a cause of one subgroup of schizophrenia. The mental disturbance might appear many years after the acute stage of the rheumatism. Observations confirming Bruetsch's evidence have been made subsequently by Van der Horst (1947) and Benda (1949). Warren and Chornyak (1947) found suggestive evidence of a causal relationship between cerebral manifestations of acute rheumatic fever and behaviour disorder. Neuberger (1947), in a clinico-pathological study of 20 children or young adults who died at the height of rheumatic fever, found two with mental symptoms which might have been related to the rheumatic fever and the lesions described.

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ANOXIA, INTOXICATIONS AND THE PROBLEM OF SELECTIVE VULNERABILITY.

The second World War stimulated much thought and experimental work on various forms of anoxia, particularly *Anoxic Anoxia* of high altitude. Fulton (1948) dealt with the physiological problems of high altitude in his series of lectures on aviation medicine. Somewhat earlier (1945) the same author, jointly with Hoff and Grenell, reviewed comprehensively the main forms of oxygen deprivation under the headings of anoxia, asphyxia, ischaemia, CO poisoning, anaesthesia and hypoglycaemia.

The most systematic single investigation into the general problem of anoxia during the period under review, has been that of Morrison (1946), on dogs and monkeys exposed repeatedly to atmospheres deficient in oxygen, which caused but transient ill-effects on single exposure. By varying the intensity of deficit and the number of exposures he was able to produce practically all the different kinds of lesion (except, apparently, of the hippocampus) which have been reported to occur in various types of anoxia: from purely grey matter lesions, such as produced by many forms of acute anoxic anoxia, to purely white matter ones, such as commonly produced by chronic sublethal anoxia. He suggested that the white matter lesions might be due either to the repetitive swing back and forth between aerobic and anaerobic metabolism upsetting enzyme system reactions in the brain, or to the chronic nature of the experiment exhausting the glucose-producing potentiality of the adrenal glands. Histologically, the fascicular layer of the adrenal cortex displayed foam cells suggesting functional exhaustion.

Pathological investigations on a smaller scale were carried out by Jensen, Becker and Windle (1948), who found focal areas of necrosis in the vermis of the cerebellum in guinea-pigs exposed 150-250 times to barometric pressures equivalent to altitudes of 30,000 ft.; by Grenell (1946), who found the isocortex to be more susceptible to damage than the allocortex after arrest of cerebral circulation in dogs; and by Titrud and Haymaker (1947), who described acute nerve cell degeneration in two fatal cases of high altitude asphyxiation among fliers.

As regards anoxic poisons, there has been little significant addition to the literature on the neuropathology of *Carbon Monoxide* since Van Liere's (1942) review, with the exception of a paper by Lewey and Drabkin (1944), who found that in the brains of dogs, after chronic repetitive exposure to the gas, the lesions were, in quality and localization, the same as in acute carbon monoxide poisoning, with the addition of frequent involvement of the white matter.

The effects of *Carbon Disulphide* on the brain of monkeys was investigated by Richter (1945), who found that repetitive sublethal exposure to the vapour for over a year produced a remarkably selective symmetrical necrosis in the globus pallidus and the zona reticulata of the substantia nigra, more exclusive than usually described in the literature on experimental carbon monoxide and cyanide poisoning. As regards pathogenesis, he left it open as to whether there may be a direct action of the gas on the nerve cells, anoxia, or an effect on enzymes, especially co-enzymes. The blood vessels showed no gross alterations.

Anoxia caused by *Anaesthetics* has been well surveyed by Hoff, Grenell and Fulton in their review already mentioned. The earlier work on this subject was fully dealt with in the previous volume (Meyer, 1944). Anoxic catastrophes due to anaesthetics have not yet, in this country, been accorded the attention which they merit in relation to the aetiology of post-operative personality changes and psychoses. It seems to be generally agreed that the brain lesions after anaesthetic catastrophes, in the case of nitrous oxide and ether at least, are essentially due to the complete or relative circulatory or respiratory failure, rather than to any substantial histotoxic action of the anaesthetics. Fletcher (1945) reported personality disintegration in 29 patients after nitrous oxide anaesthesia, and concluded that small quantities of this gas, given repeatedly, might have an accumulative effect. Meyer and McLardy tried to arouse interest in the clinical and pathological sequelae of anaesthesia, by papers read before the Psychiatric Section of the Royal Society of Medicine and the Royal Medico-Psychological Association, but the cases in point have not yet been published in full.

Anoxia related to birth injury is discussed by Dr. Norman in the chapter on the pathology of Oligophrenia. Observations on hypoglycaemia will be discussed in the section on the pathology of Physical Therapies.

There has been no significant work within the period under review on the neuropathology consequent to alcoholic *addiction*. Heilbrunn and his associates (1945) found a reduction in the number of the large cells of the putamen, and degeneration of the dentate nucleus in the brain of a chloroform addict. In three cases of morphinism, investigated by Swain (1945), the pathological findings included changes in the hippocampus and the dorsal nucleus of the vagal nerve.

Agenized flour has been shown to produce running fits in canines (Mellanby, 1946, and others), but not so far in man (Elithorn, 1949). Parry (1948) determined that the primary hysteriogenic agent is almost certainly a positive toxic substance present in the gliadin fraction of wheat protein and in certain samples of wheat flour, especially when treated by agene (NCl_3). Bentley and

his co-workers (1949) have now isolated a crystalline peptide substance which either is, or contains, the toxic factor. Gershoff and co-workers (1949), from a study of the brains of experimental dogs, concluded that there is no evidence of disturbance in cerebral oxidation or phosphorylation.

In a study of five cases of death from *Uraemia*, Knutson and Baker (1945) observed that chronic cases showed the greatest amount of perivascular demyelination and necrosis, the acute cases purely nerve cell changes. This fits in with the experimental findings with intoxicants of various kinds, that repetitive sublethal exposures over long periods divert the emphasis of structural damage onto the white matter. Baker and Knutson (1946) attributed the personality change in the five cases to the necrosis and demyelination. There was no tendency towards any special form of psychosis.

Bini and Bollea (1947) reported two cases of death from acute exposure to *tetra-ethyl of lead* in the atmosphere. They found diffuse acute degenerative changes in almost all nerve cells, and in one case additional focal lesions in the mammillary bodies and corpora quadrigemina very similar to those characteristic of Wernicke's disease. Histochemical methods of investigation did not reveal the presence of any lead. They concluded that it was not the lead, but the tetra-ethyl radicle, which was responsible.

The general problem of the *selective action* of certain toxic and other agencies is now recognized to be a very complex one, usually calling for different explanations in different cases. Symonds (1949) recently restated its fundamental importance, and Roizin (1948) reviewed the various phenomena of what he called histotoxic metabolic dysergia. No single general explanatory concept any longer satisfies all the theoretical requirements. There have been a number of specific investigations into the problem during the period under review. Perhaps the most impressive are the investigations into the toxic action of 8 amino-quinoline compounds, by Schmidt and Schmidt (1948), and Richter (1949), arising out of research into antimalarial drugs. It was found that with variations of the side-chain radicle the toxic action is quite different. Some compounds act on the heart, others on myeloid haemopoiesis, again, others on the central nervous system. Two of the compounds, plasmocid and plasmochin-sulfa, had a selective effect on the nuclei (motor and sensory) of the brain stem, the latter drug acting even more selectively than the former. The mode of action is not yet understood, but it is obvious that this and similar systematic studies hold considerable promise for the elucidation of chemical factors operative in selective vulnerability.

A chemical investigation into the vulnerability of the corpus striatum has been carried out by Lehmann and Pichler (quoted from Hassler, 1948). These authors find that the total oxygen consumption and the residual oxygen consumption, after inhibition of the iron-containing enzyme by cyanide, are greatest in the corpus striatum. This centre they found also to be richest in lactoflavin. Hassler discusses, also, work associated with other aspects of pathoclisis (the term used by C. and O. Vogt for selective vulnerability). He draws attention to the fact that, according to C. and O. Vogt, the size of the nucleolus and the number of vacuoles in this organelle is characteristic for each nerve cell group. C. and O. Vogt's and Hassler's contributions to the

problem of selective ageing of certain basal nuclei are dealt with in the section on Ageing.

The action of anoxia and anoxic poisons is one of the oldest examples of selective vulnerability, and some of at least the contributory factors (cf. Meyer, 1944) are clearer here than elsewhere. Hurst (1944) has reviewed his and his associate's earlier results of experimental cyanide and sodium azide poisoning, particularly in respect of the variation of the localization of the lesions with dosage. According to him, massive single or repeated doses usually damage chiefly the cerebral and cerebellar cortex; repeated (less often single) small doses lead to bilateral necrosis in the basal ganglia, especially the globus pallidus, or in the cerebral white matter, or in both. These results are in fair agreement with those of Morrison (1946), already quoted at the beginning of this section. Such observations, however, do nothing towards explaining, for instance, why the affection of the globus pallidus is more selective in carbon monoxide poisoning than in most other types of anoxia, why no selective necrosis of the globus pallidus has ever been reported among the ischaemic lesions following hypoglycaemia, although the latter condition very consistently affects the striate body as a whole, and why widespread degeneration of Purkinje cells is, in the experience of the writers, less frequent after carbon monoxide and cyanide poisoning, and hypoglycaemia, than after anoxia due to anaesthesia. This aspect of the problem is in process of being reviewed in the writers' laboratory.

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DEMYELINATING DISEASES.

Here again, the concept of allergic aetiology has gained considerable ground. *Acute disseminated encephalomyelitis* is now widely believed to be an allergic encephalopathy. The experiments and conclusions of Kabat and his associates

and of Morgan have already been mentioned in the section on Inflammatory Diseases. Ferraro and his co-workers (1944, 1945, 1948a, 1948b, 1949) have further, shown that by injection of an emulsion of homogenous brain and old tubercle bacilli, they can produce in monkeys a demyelination and a glial reaction which seems to approximate to the appearance of the lesions in human disseminated sclerosis. They contemplate the use of still more attenuated emulsions. Working along similar lines, Morrison (1947) has created disseminated areas of demyelination in rabbit brains by injection of homogenous antigens. Koprowski and Jervis (1948) produced the same in guinea-pigs by inoculation of brain tissues (and adjuvants) derived from five different mammalian species. Ferraro and Cazzullo (1949) have now gone on to devise a method of protection against this form of experimental allergic encephalomyelitis—by the previous injection of a pure brain emulsion. They suggest that the principle may lead to ways of preventing neurotropic virus infections. Finally, it may be mentioned that Van Bogaert (1948a, b), in reviewing the “maladies de la substance blanche,” disseminated sclerosis in particular, found that many of the clinical observations accord with an allergic conception.

As regards *disseminated sclerosis*, many theories other than the allergic one have continued to receive support during the period under review. Margulis and co-workers (1946) have brought further support to the infective theory by claiming to have demonstrated experimental infection with viruses from sera derived from patients with disseminated sclerosis. In his review of the various aetiological theories, McAlpine (1946) also showed at least a slight preference for the infective theory. The theory of a deficiency as well as infective factor was revived dramatically by Campbell and his associates' (1947) report of organic disease resembling disseminated sclerosis developing in technicians engaged in research work on the prevention of swayback in sheep by copper therapy. Mandelbrote and his associates (1948), however, have had negative results so far in their exploration of the possible relationship of human disseminated sclerosis with copper metabolism. A metabolic theory has been postulated by Weil (1948), and Weil and Bradburne (1948). From observations of severe depletion of phosphorus in both grey and white matter of the brains of disseminated sclerosis patients, and accumulation of phosphorus in the proliferated glia, they deduce that the cause of myelin destruction is a slow metabolism of phospholipid, the phosphorus being retained in the glia and not transmitted to the myelin, which consequently breaks down. Scheinker's (1943) vascular hypothesis of the pathogenesis of the early lesions in disseminated sclerosis has already been mentioned in the Section on Vascular Diseases. Theories that myelin loss may be mediated by an enzymatic derangement, are enhanced by Morrison's (1946) and Hurst's (1944) experimental production of demyelination by repetitive small exposures to anoxia and histotoxic poisons, respectively, over prolonged periods. Morrison suggested that the swing from aerobic to anaerobic oxidation may be the factor responsible. Hurst conceived the effects to be due to deficiency in oxidase ferments in the white matter. King and Meehan's (1948) critical review of spontaneous demyelinating diseases of animals re-emphasized that “demyelination” is

not a specific disease due to a single cause, but a general type of response of white matter to noxious stimuli. They compare it with "fever" in general medicine.

As regards other special forms of demyelinating disease, two fresh cases have been reported (Friedman and Davison, 1945; Roizin, Moriarty and Weil, 1945) of the *intermediate group* which falls, in severity, between ordinary disseminated sclerosis and Schilder's Disease, and which, occurring in an older age group than the latter, manifests more prominent, earlier, mental symptoms. Three such cases (unpublished) have been investigated in our laboratory. In all three severe organic dementia developed several years before neurological abnormalities (except fits in one case) became apparent. Morphologically, the lesions displayed more continuous demyelination and more extensive fibrous gliosis than in ordinary disseminated sclerosis, and the destruction of axis cylinders was more severe.

What is apparently the first case of *Marchiafava's Disease* (Primary Degeneration of the Corpus Callosum) seen in this country, is under investigation in our laboratory. All 46 cases reported in the literature have occurred either in Italy or in the U.S.A., all but two in Italians (Bohrod, 1942; Nielsen and Courville, 1943), and all but one in chronic alcoholics. Investigation, so far, of the present case has revealed no suggestion of Italian genealogy or of indulgence in Italian crude wine. Nor is there any history of trauma as found by Merritt and Weisman (1945) in the fourth and fifth American cases.

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NUTRITIONAL DEFICIENCIES.

The promise which earlier studies of the vitamin deficiencies seemed to hold out for elucidation of the pathogenesis of the acute nutritional deficiency encephalopathies, and the larger group of symptomatic psychoses such as the

alcoholic psychoses, has not been realized by the work of the past five years. Advance has been largely in the direction of confirmation of previous findings, determination of precise origin of vitamin deficiencies, and extension of deficiency researches to other essential foodstuffs.

Instructive reviews have been written by Youmans (1943) and Follis (1948) on the whole medical and experimental field of deficiencies in vitamins and essential elements, amino acids and fatty acids; by Ershoff (1948) and Leitner (1948), on secondary, or "conditioned," deficiencies; by Eddy and Dalldorf (1944) and Bicknell and Prescott (1946), regarding the vitamin factors alone; and by the Association for Research in Nervous and Mental Diseases (1943), Spillane (1946) and Denny-Brown (1947), on the main nutritional deficiencies affecting the nervous system. The circumstances of prisoner-of-war life promoted a wealth of clinical observations, especially on vitamin B deficiencies, but gave little opportunity for histopathological investigation.

Ellinger and his co-workers (1944a, b) demonstrated that vitamins are synthesized by micro-organisms in the human gut, and that up to 80 per cent. of the human requirements of nicotinic acid may be manufactured thus. Benesch (1945), from studies of normal caecal flora producing and destroying nicotinic acid, conceived that upset of the equilibrium between these two processes might play a part in the causation of deficiency diseases. Hardwick (1946) made the interesting clinical deduction that upper intestinal abnormality may result in thiamine deficiency, lower intestinal disease in nicotinic acid deficiency. Ellinger and Shattock (1946) made clinical observations on the sterilizing effect of orally administered penicillin, as well as sulpha drugs, on nicotinic acid elaboration in the gut. Darkening of the tongue featured among the symptoms in each case. It may prove relevant to recent biochemical studies on the central nervous system that Bruno (1946) has produced experimental evidence that thiamine may play a part in the synthesis of acetylcholine.

Pink disease (acrodynia) has become accepted by many as a deficiency disease related to *pellagra*. Fisher (1947), in a review of 65 cases with two autopsies, was unable to throw any light on the pathology. Denny-Brown (1947) considered it a part of the syndrome of *pellagra* which could occasionally occur independently and could be cured by pantothenic acid therapy. Raska (1947) produced experimental *pellagra* (black tongue) in dogs by excess oral dosage of adenine, which he considered might act by interfering with the formation of nucleoproteins. No definite and selective retrograde cell changes have as yet been demonstrated experimentally, either by the withholding of nicotinic acid from the diet or by enzyme blocking by, for instance, acetyl pyridine.

Pathological studies on *Wernicke's encephalopathy*, by Meyer (1944), Riggs and Boles (1944), Barrie (1947), Wardener and Lennox (1947) and others, largely confirmed previous findings. Meyer drew attention to the apparent negative correlation between the neuropathology of this syndrome and of *pellagra*. Whether this may be related to Hardwick's observation (just mentioned) remains to be seen. Degeneration in the dorsomedial corner of the inferior olives was an unexplained feature of 4 out of 5 of Meyer's fully investigated cases. One case displayed degeneration in the granular layer of

the cerebellum. The latter phenomenon has been more fully studied by Leigh and Meyer (1949) in cases of visceral carcinoma, fatal hypoglycaemic coma and amaurotic idiocy. No clue of any specific deficiency factor was discovered from the available information. The only common factor appeared to be terminal cachexia.

So far the only fully investigated case suspected to be one of predominantly *riboflavine* deficiency (Spillane, 1946) revealed only moderate necrosis of the Sommer sector of the hippocampus, and some degree of chromatolysis in the Betz cells. Stannus (1944, 1948), from dubious premises, speculated on the interference of *riboflavine* deficiency with the normal functioning of brain capillaries and of glucose metabolism in the neuropil, leading to tissue anoxia affecting first the nerve cells with highest metabolic rate.

Pyridoxine (B6) and *Pantothenic acid* have been the subject of experimental investigations by Swank and Adams (1948), and Follis (1948). Swank and Adams concluded that deficiency in either of them can impair the metabolism of the same types of nerve cells as can thiamine deficiency, producing similar pathological changes (and ataxic symptoms). Follis concluded that *pyridoxine* is probably concerned with the metabolism of the myelin of sensory nerves, *pantothenic acid* with the metabolism of the body of sensory nerve cells. He deduced also that the metabolism of motor and sensory peripheral nerves must be different. Bodian's (1948) observations on the effects of desoxypyridoxine treatment on the infectivity of monkeys by poliomyelitis has already been mentioned in the section on Inflammatory Diseases. Denny-Brown (1948) considered that in two cases of bronchogenic carcinoma with primary sensory neuropathy, the degenerative changes found in the dorsal root ganglion cells might be due to toxic upset of *pantothenic acid* and/or vitamin E metabolism. Hagerman and Hirschfeld (1947), from studies of early evidence of vitamin B deficiencies, by means of the disappearance of the fluorescent coating of the tongue as seen under ultraviolet irradiation, concluded that *pantothenic acid* deficiency was probably the vitamin B factor most responsible for the phenomenon, but offered no suggestion as to its biological basis.

Vitamin B 12 is now considered (Berk *et al.*, 1948; Leader, 1949a, b) to come close to being the ultimate anti-anaemic principle. There has been no report to date on histopathological findings after its clinical cure of the symptoms of subacute combined degeneration. Cerebral changes in the course of *pernicious anaemia* have been described in two new cases by Adams and Kubik (1944), and in seven new cases by Ferraro, Arieti and English (1945). The former workers concluded that the brain lesions are identical with those in the cord, and that when definite and diffuse they are always (on the evidence of their own two cases and twelve in the literature) accompanied by mental symptoms. The latter workers concluded that the commonest mental symptoms comprise a paranoid psychosis often indistinguishable from paranoid schizophrenia.

Synthetic *biotin* has been successfully employed by Smith (1945) in the cure of progressive paralysis in dogs caused by vitamin-B-complex-deficient diet supplemented by all the other known B factors. The nature of the defect caused in the nervous system remains obscure.

Amino-acid deficiency studies are only in their beginning. Findings, so far, with bearing on diseases of the central nervous system comprise the observations by Himsworth (1946/7) and his associates (1945) of anorexia in rats caused by methionine deficiency in the diet; and several observations on hepato-cerebral diseases:

In an early case of the clinical pseudosclerotic type of *hepato-lenticular degeneration*, Uzman and Denny-Brown (1948) demonstrated the continuous and abnormal presence of aminoaciduria (including alanine, glutamic acid and aspartic acid) in the absence of evidence of renal disease. Liver biopsy was negative, but Kayser-Fleischer rings were present, and the patient's elder brother also displayed almost identical neurological signs. The authors favoured the concept that the manifest disease is due to a basic defect in the metabolism of amino-acids rather than to failure of deamination due to primary impairment of liver function. This view would tend to bring the usual hepatic concomitant into line with Himsworth and Glynn's (1944) demonstration of trophopathic hepatitis caused by experimental dietary deficiency in a component of protein. Cumings (1948), from his findings of abnormally high copper and low iron in certain parts of the brain, in three cases of *hepato-lenticular degeneration*, also favoured its classification as a metabolic disease. Baker (1949) considered that the predominantly perivascular distribution of nerve cell and myelin degeneration in his eight cases of liver disease, when taken with experimental findings, most notably those of De Jong (1945), favoured the view that liver damage enables some endogenous toxin, most probably liberated from the intestine, to reach the brain. Leigh and Card (1949) have observed the combination of pseudosclerotic *hepato-lenticular degeneration* with the type of cord changes which have been described in the ataxic form of pellagra. These authors favour the alternative view that deficiency of a liver principle is the causal factor relating liver disease to the brain changes.

Ferraro and Roizin (1943) produced widespread diapedetic haemorrhages in the brains of chickens and cats by feeding diets deficient in *vitamin K*. Young animals were most susceptible. They considered that lack of prothrombin probably alters the hydro-dynamics of the vessel wall.

Although no definite deficiency factor has so far been demonstrated in *porphyria*, it is perhaps appropriate to deal with this condition here. In one case which came to autopsy, Denny-Brown (1945) found ischaemic lesions in the cerebral white matter as well as in the peripheral nerves. He thought this might be evidence of some locally acting vasoconstrictor substance. Baker and Watson (1945) emphasized the frequency of mental disturbances, usually in the form of toxic delirium or severe depression, and of evidence of neuronal and myelin sheath alterations throughout the brain as well as the spinal cord. A review of the literature and their one personal case suggested some selective vulnerability of the 7th and 12th cranial nerves as well as the dorsal nucleus of the 10th, the latter being presumably responsible for death in fatal cases. Marchand and Ajuriaguerra (1949) reviewed all the cases in the literature containing a complete study of the central nervous system, and found chromatolysis, especially in nerve cells of the medulla and Clark's column in their personal case. Levy and Perry (1949) consider that no report has yet

appeared in which the mental manifestations were of primary importance and dominated the clinical picture.

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AGEING, SENILE AND PRESENILE DEMENTIAS AND SYSTEM DISEASES.

The growing realization in the United States and this country, of the ageing trend in the distribution of the population has already focussed much new attention on gerontological and geriatric problems. Journals covering both the general subject and the more restricted medical field have commenced publication during the period under review. *Biological Symposia*, Volume 11 (1945), is devoted to a symposium on "Ageing and Degenerative Diseases," by leading American workers on geriatric problems.

Nutritional factors in ageing have been studied by Saxton (1945), who

demonstrated a 50 per cent. increase in the longevity of rats fed on diets considerably less in amount than they spontaneously consume, but complete in all the known essentials. Mills (1948) confirmed that ageing animals show an increasing demand for thiamine. Korenchevsky (1949) reviewed briefly some of the problems of gerontological research, especially in relation to nutritional experiments and investigations into auto-intoxication.

As regards *endocrine factors*, this last author (Korenchevsky, 1948) has also summarized the work of his research unit on countering involutional ageing after ovariectomy in rats by means of pluri-hormonal treatment. Another example of the halting of some signs of ageing by endocrine action has been furnished by Thomson (1949), whose biochemical research team has found that an alteration in the pattern of blood-chemistry in apparently healthy old men (reduced sodium and chloride; delay in hypoglycaemic response to insulin; defective vitamin C storage; and diminished keto-steroid excretion) can be restored to normal by injections of testosterone. Timiras and his associates' (1949) production of marked hyalinization and necrosis in cerebral vessels by overdosage of animals with desoxycorticosterone has already been mentioned in discussing work related to periarteritis nodosa. Safford and Gellhorn (1945) have shown the excitability of the sympathetic-adrenal system (in rats) to decrease with age, unlike that of the vago-insulin system.

No correlation between *arteriosclerosis* and age was observed by Hirsch (1945) in 2,051 brains, and no sign at all of arteriosclerosis in 9.5 per cent. of autopsies in 400 old men over the age of 65. He concluded that arteriosclerosis is a malady, not of old age, but of civilization. Riese and Zfass (1944) reported detailed histological findings in the brain of a man who died at the age of 107, after displaying signs of senile dementia for 11 years. The cortical cyto-architecture was well preserved in all the numerous areas studied, although other signs of age, such as senile plaques, were present. This must have been an exceptional case of senile dementia. Riese (1946), in a further report on very limited parts of the cortex of this and 17 other human brains from patients dying between the ages of 77 and 107, like Hirsch, found no correlation between arteriosclerosis and age; nor any between age and diffuse or regional cortical atrophy, nerve cell changes, satellitosis, or duration of the terminal dementia or psychosis. The cytoarchitecture in the three regions examined in all 18 cases was well preserved, except for occasional palings and small softenings.

C. and O. Vogt (quoted by Hassler) and Hassler (1948) described two types of ageing of nerve cells, one with increase of lipofuscin, the other with shrinkage and lightening of the whole cell. They found relatively early occurrence of these in Meynert's sublenticular nucleus and in the centromedian nucleus of the thalamus.

By the use of a precise optical method for the detection of amyloid, Divry (1947) demonstrated that Alzheimer's fibrillar degeneration within nerve cells and senile plaques are, like the changes in the media of vessels in old age, due to infiltration by amyloid, this being a colloidal precipitate derived from the "milieu interstitiel" by transformation of sol into gel. His general views closely follow the well-known hypothesis on ageing of von Braunnühl, Ruzicka and Alexander.

There have been several reports relating to the pathology of *presenile disease*. Newton (1948), from a study of 150 consecutive autopsies (111 of the patients being over 50 years of age) at a mental hospital, concluded that senile plaques constitute the basic histological finding in *senile dementia* and *Alzheimer's disease*, but found no statistical evidence to suggest that the plaques determine the occurrence of the dementia. He concluded that the brain in Alzheimer's disease, senile dementia and senility shows essentially the same histopathological changes, simply developing at different ages, and perhaps more frequently in posterior parts in Alzheimer's disease. Senile plaques tended to occur in females earlier, and four times as frequently as in males. They must be very profuse in a particular area to produce localizing symptoms. In only four instances were Alzheimer's neurofibrillar whorls present in the absence of senile plaques. On the other hand, Mutrux (1947), from a study of six brains from cases of Alzheimer's disease and four from senile dementias, concluded that the localization of the lesions differed in the two conditions, and that he could differentiate two clinical syndromes of Alzheimer's disease corresponding to histopathological differences.

Two cases of *Pick's Disease*, studied by Malamud and Waggoner (1943), were considered to add to the evidence for dominant inheritance of the condition, and to support the concept that it is a system disease of the phylogenetically youngest cytoarchitectural regions. Akelaitis (1944) described a case which he considered opposed this latter view because of the severe degeneration throughout the caudate nucleus. Two cases in favour of the view that there may be conditions intermediate between Pick's and Alzheimer's disease have been quoted by Berlin (1949). Neumann (1949) has recently offered a clarification of some of the inconsistencies in the neuropathological literature on Pick's disease by her suggestion, derived from the clinico-pathological study of seven personal cases, and a review of over 200 cases in the literature, that there are two distinct histo-anatomical types of Pick's disease. Type I is characterized by marked focal cortical devastation with loss of nerve cells and axis cylinders. Remaining nerve cells are swollen and may exhibit eccentric nuclei and argyrophilic cytoplasmic inclusions. There is astrogliosis of the cortex, and isomorphous fibrillary gliosis of the white matter. Demyelination and reactive gliosis parallel each other in severity. Damage to subcortical centres is not prominent. Polar regions, frontal or temporal, are mainly affected. Type II is characterized by widespread gliosis, cellular and fibrillary, of the subcortex out of proportion to demyelination of these areas. Cortical damage is less prominent and alterations in the nerve cells are non-specific. Subcortical centres are frequently involved, including degeneration of descending motor tracts. The atrophy is generally not polar in distribution. Disturbances are observed in motor and sensory spheres rather than in structures associated with "higher" mental processes. She suggests that the two types have different aetiologies, Type I being due to some noxious agent acting primarily on the parenchyma, Type II due to primary disease of the astroglia.

Little advance has been made regarding the pathogenesis of the so-called *system diseases*. *Jacob-Creutzfeldt's disease* was diagnosed in two cases which

Stengel and Wilson (1946) considered might be due to deficiency disease. In one of them senile plaques were described for the first time in the literature of the syndrome. "The role of psychosis in *amyotrophic lateral sclerosis*" was discussed by Friedlander and Kesert (1948), in reviewing 34 cases in the literature, and one new case, without arriving at any definite conclusion. Van Bogaert and Borremans (1947) described two brothers with *cerebellar atrophy*, who developed a confusional syndrome ending in dementia. They considered these mental changes most probably attributable to vascular changes found in the cerebral cortex and elsewhere. From a study of two cases of *Huntington's Chorea*, Dogliani (1947) concluded that proliferation of the intima, fatty degeneration of the media and fibrosis of small vessels was the essential pathogenic feature of the condition. McLardy (1948) described retrograde nerve cell shrinkage and gliosis in the centromedian nucleus of the thalamus in cases of *Huntington's Chorea*, proportional to the cell loss in the striatum, to which the centromedian nucleus is considered to project.

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CEREBRAL TUMOURS, TRAUMA AND LOCALIZATION OF MENTAL FUNCTION.

Cerebral Tumours.

Tumours in localities where lesions cause few localizing neurological symptoms or signs are prone, in their early stages at least, to cause mental symptoms or personality changes which result in admission to psychiatric clinics and wards. Again, the severity of the mental concomitants may simply obscure the neurological signs. In five such cases of *masking brain tumours* by mental symptoms, Gottesfeld (1945) identified a common trend towards depression with anxiety, rapidly alternating with apathy, irritability and jocosity, although the nature and position of the five tumours (all cortical) was very variable. Brock and Wiesel (1949) gave a description of four cases where neurotic and psychotic symptoms dominated the clinical picture during the

early months of the illness, leading to a diagnosis of functional brain disease and treatment by E.C.T. Two proved to have temporal lobe tumours, one a frontal tumour and one a medullary tumour. The early symptoms were general and varied, and even in retrospect did not suggest specific local dysfunction: (an electroencephalogram had been taken in three). Erickson (1945) described a patient with ten years' history of episodic erotomania and diagnosis of nymphomania, where subsequent operation revealed a haemangioma of the right paracentral lobule.

Probably the type of intracranial tumour which most commonly eludes neurological (including electroencephalographic) diagnosis is the *diffuse glioma*. The histopathology of such diffuse gliomata was the subject of a monograph by De Busscher and Scherer (1942), which has only become generally available since the end of the war. From their very full and detailed study of 135 astrocytomas they concluded that such tumours are always diffuse and polymorphic in cell type, often displaying in different places the whole gamut of tumour types related to the astrocytic glia. In consequence, they stressed the inadequacy in such cases of sample histopathological (histogenic) diagnosis. In the course of three years, in a relatively small turnover of tumour material, the writers have seen three such cases admitted to mental hospitals with the diagnosis of hysterical headaches, hysterical amnesia and presenile dementia, respectively. Scheinker and Evans (1943) reviewed the literature on these "diffuse cerebral glioblastoses," and added three personal cases, in one of which mental changes were the conspicuous early features. They considered the condition to approximate to the blastomatous type of Schilder's disease.

De Busscher and Scherer also concluded that there is no such entity as a pure oligodendrocytoma, all adequately investigated cases of their own, or in the literature, showing mixture with astrocytoma, ependymoma or other form of glioma. Blumenfeld and Gardner (1945) did not comment upon this point in their review of 12 cases of "disseminated oligodendroglioma," but emphasized their ventricular and/or subarachnoid spread and noted that disturbances of behaviour were prominent features in eight of them. The present writers have recently investigated one such mixed oligodendro- and astrocytoma in which the presenting symptoms consisted of irritability, migrainous headaches and increasing apathy. Until 3 weeks before death she was considered to be a case of either simple schizophrenia or hysteria.

Another, rarer, often diffuse brain tumour is the condition called *microgliomatosis*, described for the first time, in seven cases, by Russell, Marshall and Smith (1948). The microglia, previously considered immune from neoplastic change, is considered by these observers to be participating here in a general reticulosis; the histological features in the brain comprising aggregates of diffusely intermingled proliferating cells, some of which possess the nuclear and staining characteristics of microglia. Three of the seven cases displayed progressive drowsiness and lethargy as prominent symptoms, but all showed other signs of rapidly advancing intracranial tumour.

As regards recent advances in the descriptive classification of brain tumours of more remote interest to the psychiatrist, there are several papers which deal with the subarachnoid or ventricular spread of gliomata (Tarlov and Davidoff,

1946; O'Connell, 1946; Rupp, 1948). Russell and Cairns (1947) have re-established their belief in the existence of an entity usefully separated off from other gliomata as "polar spongioblastoma," but different from what has previously been understood by this term.

Cerebral Trauma.

Several recent studies on head injuries have directed attention to regions now recognized to be intimately concerned in the auto-expressive aspects of personality, notably the orbital regions and the hypothalamus. Holbourn (1943), by demonstrating the importance of the rotatory motion of the head in the production of contre-coup injuries, stressed the inevitable high frequency of bilateral orbital damage (and hence of personality change). Puech and Mallet (1946/7), from a correlation of the occurrence of mental symptoms and of gross organic lesions in 54 cases of cerebral trauma, concluded that a prerequisite to psychiatric, as distinct from neurological or epileptic, symptoms seemed to be diffuseness of the lesions and concurrent involvement of cortex, hypothalamic and bulbo-pontine structures, such as are especially liable to occur in traumatic acceleration or deceleration of the head. They also noted that prefrontal orbital lesions seemed associated with the appearance of aggressiveness, comparable to the sham rage in animal experiments; and that damage to the right frontal lobe was more inducive to psychic and intellectual disturbances than damage to the left one. Scheinker (1947) suggested that traumatic herniation of the brain stem through the tentorial opening might cause the common post-traumatic neuro-vegetative disturbances by interrupting diencephalic-medullary connections.

A "punch drunk" syndrome was produced in rats by Tedeschi (1945) by means of repeated blunt impacts of subconcussive intensity applied to the head. Histologically, he found disseminated focal rarefaction and degeneration of cortical nerve cells, of axons and of myelin, with glial proliferation in the later stages. The damage was proportionate to the strength and number of blows. He concluded that concussion may be due to detectable neuronal injury. The immediate excitatory phenomena following severe head injury were attributed by Bornstein (1946) to liberation of abnormal amounts of acetylcholine, some of which escaped into intercellular spaces as well as into the cerebrospinal fluid. Spiegel, Spiegel-Adolf and Wycis (1946) demonstrated that cerebrospinal fluid from concussed patients had a chromatolytic action on the anterior horn cells of cats, thus corroborating their previous spectrographic evidence that the cerebrospinal fluid of concussed animals and human beings probably contains a ribo-nuclease substance.

Finally, mention should be made of Scheinker's (1947, 1949) view that the ultimate pathogenesis of cerebral "tumefaction, oedema and liquefaction" lies in functional vascular disturbances; of Le Beau's (1948) demonstration of acute oedema caused by experimental lesions in medial regions between mid-medulla and posterior hypothalamic areas; of Hallervorden and his associates' (1948) conception of concussion as a colloidal disturbance called "thixotropic"; of the widespread nerve cell changes, which Courville and his associates, Rand and Bloomquist (1944, 1945, 1946, 1947), considered may

persist for some time without irreversible change and provide the structural basis of post-concussional syndromes; and of the 27 papers on "Trauma of the Central Nervous System," published in Vol. 14 of the *Proceedings of the Association for Research into Nervous and Mental Diseases* (1945).

Localization.

In the period under review the growth of psychosurgery has focussed attention on the frontal lobes, but frontal lobe function cannot be dealt with in isolation. The prefrontal region has intimate connections with the thalamus, particularly the dorso-medial nucleus and direct connections, as well as indirect ones, through the thalamus with the hypothalamus, which, in its turn, is connected with the cingular gyrus through the anterior nucleus of the thalamus, and with the hippocampal region through the fornix system. It will be noted that these regions mentioned include most of the centres which, in lower mammals, Papez (1937, 1940) presented as a "well interconnected and harmonious mechanism which may elaborate the functions of central emotion as well as participate in emotional expression." Many of these centres were previously considered to be concerned with smell, but evidence is rapidly growing that they have no such function in higher mammals.

It is now nine years since prefrontal leucotomy was introduced into this country, so that brains from patients who survived the operation and died of intercurrent illness begin to become available for study. They provide valuable material for the correlation of clinical changes with circumscribed surgical lesions. So far as such studies pertain to elucidation of mental functions of the *frontal lobes*, Meyer and his associates (1947; 1948*a, b*; 1949*a, b*) have failed to find any evidence of the atomistic parcellation of function in the prefrontal regions suggested by Kleist, or even of its simplified form proposed by Dax and Radley-Smith (1946); nor of Freeman and Watts' (1948) more dynamic concept of creative artistry being located in the frontal poles. In their series of some 70 cases with over six months' survival, no substantiation could be found even of the widely held belief that damage to the orbital regions is particularly associated with a euphoric type of personality change. Information regarding the premorbid personality of the patient was inadequate for correlation. The severity of the personality change (usually of the apathetic, akinetic type) appeared to be proportional to the quantity of cortex isolated from its long fibre connections.

Lesions infringing upon white or grey matter of the band of dysgranular and agranular cortex, comprising Brodmann's areas 8, 6, posterior 9, posterior 47, 13, and the anterior cingulate gyrus (area 24) were found by Meyer and his co-workers to be associated significantly frequently with clinical reports of *autonomic disturbances*. Such findings were to be expected from, for instance, the experimental observations of Livingston and his associates, on stimulation and regional ablation of the orbital surface of the frontal lobe in monkeys (1948*a*), and stimulation of this region prior to leucotomy in man (1948*b*). The clinical reports seldom describe such severe mental or physical changes, however, as might have been anticipated from Smith's (1945), Kremer's (1947) and Ward's (1948) experimental observations on the cingulate gyrus, and Ruch

and Shenkin's (1943) and Fulton's (1947) findings (of hyperactivity) in monkeys after bilateral damage to posterior orbital cortex. It may be noted that Ruch and Shenkin's and Fulton's observations were not confirmed by Bard and Mountcastle (1948), whose experimental cats remained placid after removal of all neocortex outside the rhinencephalon; that Pool (1949) and Scoville (1949) found no striking mental changes in patients submitted to bilateral ablation or undercutting of area 24; and that Mettler (1945), like Richter and Hines (1938), concluded that to produce hyperactivity in monkeys the striatum must be damaged. It may be mentioned, in passing, that several cases where the leucotome had been inserted through even posterior parts of area 44 on either side had no clinical record of speech defect.

The psychological sequelae of *thalamotomy* have not yet been reported in detail, though it is claimed that the operation results in a minimal personality change (Spiegel and Freed, 1949). A case of progressive dementia due to bilateral circumscribed atrophy of essentially the dorsomedial nucleus of the thalamus, was recorded by Grünthal (1942), and exaggerated reaction to emotional stimulation was described by Engel and Aring (1945) in a case of old cystic degeneration destroying the ventral half of the right dorsomedial nucleus.

Most of the literature referring to sham rage of hypothalamic origin is of earlier date. It was critically reviewed by Masserman (1943), who emphatically rejected localization of emotional experience, as distinct from emotional expression, in the *hypothalamus*. This view received further support from David, Hecaen and Talairach (1946) who, from a study of mental disorders of expansive type in the course of intervention in the region of the third ventricle, concluded that interference with anterior diencephalic regions is not by itself sufficient to cause such mental symptoms: there must be a supplementary factor originating in prefrontal cortex, probably orbital cortex. Pedersen (1948), on the other hand, attributed to the vegetative centres in the hypothalamus a "rather uniform emotional syndrome, featuring instability and egocentricity," often called "hysterical," which he observed in both a group of patients with pituitary lesions and a group with hypothalamic lesions. He considered that the material bore out the theory of the great importance of the hypothalamus for emotional disturbances and hysterical reactions. Wheatley (1944) determined that all his experimental cats which became savage had lesions in the ventromedial nucleus of the hypothalamus, whilst bilateral fornix lesions did not alter their affective behaviour.

Spatz and his associates (quoted from Wordehoff, 1948) have concluded, from clinical and experimental observations, that the *tuber cinereum* near the infundibulum has influence on sexual functions. Papez and Ecker (1947) described a personal case which they considered "adds to the growing body of evidence that precocious puberty in males may result from certain lesions in the posterior portion of the hypothalamus." Theirs was a case of an intraventricular infundibuloma arising just in front of the mammillary bodies.

The relationship of Korsakoff's Syndrome to the hypothalamus has been investigated afresh by Morsier and Rey (1945) and Brouwer (1948). The former noted it in two cases, one of a meningioma pressing bilaterally on the

posterior orbital region, the other of a chromophobe adenoma of the pituitary. In this last case the Korsakoff Syndrome of ten years' duration recovered completely after operation on the tumour. Brouwer found it in four of ten cases of hypothalamic lesions, and confirmed that the mammillary bodies and their immediate entourage are implicated in its genesis.

The problem of *consciousness* and its localization has been critically reviewed by Jefferson (1944) and Martin (1949).

The relation of the *cingulate region* to behaviour has been experimentally investigated, especially by Smith (1945) and Ward (1948). Both concluded that it is intimately related to emotional expression, particularly fear. So far, psychosurgery in the human brain has not materially substantiated these claims. Ward concluded that mental symptoms, when they occur after lesions to the *corpus callosum*, must be attributed to involvement of the adjacent cingulate gyri, interruption of the corpus callosum itself not being followed by mental symptoms (Akelaitis, 1941). De Busscher and Scherer, on the other hand, concluded from one case of their own and a review of the literature, that there undoubtedly exists a characteristic psychiatric "callosal syndrome," with accessory neurological symptoms. It features, in its early stages, a depressive state, loss of initiative, loss of co-ordination of ideas, eccentricities of posture and other bizarre behaviour. It can follow a relatively minimal lesion of the anterior part of the corpus callosum, such as in their case of a mixed oligodendro-astrocytoma, which issued into the ventricles from the posterior surface of the genu, causing no extensive destruction even to the corpus callosum. It might be that irritative pathological lesions of callosal fibres create more dysfunction than do clean surgical lesions. In this connection it is also of interest that French and Bucy (1948), in a review of five personal cases and 31 cases in the literature, of tumours of the *septum pellucidum*, found the commonest symptoms to comprise episodic headaches, visual and oral symptoms, cataleptic-like weakness, memory changes and occasional convulsions.

Bard and Mountcastle found the bilateral removal of the *hippocampus*, in extensively decorticated cats, to augment their pleasure reactions so long as the amygdaloid nuclei were spared. Substantial additional damage to the amygdala (or of anterior cingulate cortex) resulted in an extraordinary and lasting depression of the threshold to rage reaction after a latency of several weeks. They considered this finding incompatible with Bucy and Kluver's (1940) observations in monkeys, although it is not at all clear that damage to the amygdala was of the same order in the two sets of experiments. It confirmed the observations on the amygdaloid nuclei by Spiegel, Miller and Oppenheimer (1940).

Frantz (1947) has made a comprehensive review of the literature bearing on psychiatric manifestations of *temporal lobe* lesions. He calls right temporal lobe tumours "imposters," in virtue of the frequency with which they simulate lesions of the frontal lobe, often producing even *Witzelsucht*. He was impressed by the high incidence of reduction in drive and slowing in mental tempo after ablation of the right temporal lobe.

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FUNCTIONAL PSYCHOSES.

These, in principle, comprise the schizophrenias, the paranoid psychoses, the manic-depressive group and idiopathic epilepsy. Certain forms of mental deficiency should be included, but these are dealt with separately in the chapter on the Pathology of Oligophrenia. Epilepsy has now become largely an electroencephalographic problem. Comprehensive reviews of the pathological literature have been given in the monograph by Bellak (1948), and in a thesis on "The Somatic Manifestations of Schizophrenia," by Shattock (1949).

The old vexing question as to whether there is a substrate in the schizophrenic brain recognizable by the application of ordinary histological methods, is still receiving widely different answers. While, in the previous period reviewed (Meyer, 1944), the trend of opinion seemed to deny the existence of such an organic substrate, more recent contributions show a more positive attitude, although the evidence brought forward in support is far from decisive. The finding by Elvidge and Reed (1938), of swelling of the oligodendroglia, exclusively in biopsies taken from the brains of psychotic individuals, has not been re-examined, although the findings are often quoted. In our laboratory the oligodendroglia has been investigated in biopsies of the cerebral white matter obtained from eight psychotics during leucotomy. It was found that the appearance of these cells (after application of the method used by Elvidge and Reed) varied considerably from individual to individual, normal oligodendroglia occurring in the same brain together with others in various stages of swelling. In biopsies taken from three mentally normal control cases so far available for investigation, but fixed in ordinary 10 per cent. formalin, no swollen oligodendrocyte was seen. This investigation is obviously not yet completed, but, from the results so far, one may conclude that there seems to be some difference between the mentally normal and abnormal cases, and also considerable quantitative and qualitative variation within the group of psychotics. Swelling of the oligodendroglia is known to be a labile process occurring consistently after even the shortest period of post mortem autolysis. Such a labile phenomenon is unlikely to be the "substrate" of a chronic psychosis, but if confirmed may have some secondary significance.

Kirschbaum and Heilbrunn (1944), in cortical biopsies obtained during leucotomy on schizophrenics, found degenerative changes in the nerve cells and proliferation of astrocytes which were not present in control cases. Likewise, Hyden and Hartelius (1948), as already mentioned in another section, found what they believed to be a significant difference in the quantity of nucleotides in the nerve cells of schizophrenics (obtained by biopsy during leucotomy) as compared with the amount in nerve cells of normal brains studied post mortem. These authors, however, did not pay sufficient attention to the well-known peculiarities in the appearance of nerve cells in biopsy specimens. Their results are therefore extremely doubtful. Special care in the interpretation of cortical biopsy specimens has been advocated by Meyer and Meyer (1945, 1949).

There have also been a number of reports on post mortem studies of the brains of schizophrenic patients (Frey, 1948; Vogt and Vogt, 1949; Winkelman

and Book, 1949). The report of the last-named authors is the most comprehensive. It was based on the findings in ten "typical cases of schizophrenia." The changes found were similar in nature to those seen in the biopsy specimens of Kirschbaum and Heilbrunn, but exceeded in intensity anything so far reported under the heading of schizophrenia. One wonders whether some of these cases may not have been organic psychoses with schizoid episodes, of a type which has been reported by, for instance, Ferraro (1943), Hoft and Tedeschi (1943), and Roizin, Moriarty and Weil (1945), where some proved to be cases of Schilder's disease simulating schizophrenia.

In the ten cases of Winkelman and Book the brain was reported to be macroscopically normal. This contrasts with recent reports (Puech, 1949; Pool, 1949) of macroscopic anomalies of the frontal cortex and meninges observed during psychosurgical operations. It also contrasts with pneumoencephalographic findings (Donovan, Galbraith and Jackson, 1949) of an "atrophy" of the schizophrenic brain, and with the claim of several neurosurgeons (so far reported mainly verbally) to have observed marked cerebral atrophy at leucotomy operation. It will be remembered, in this connection, that the school of Rieger and Reichardt many years ago investigated the ratio of skull capacity to brain volume, and found among certain psychotic patients interesting variations from the normal. It might well be that further investigation along such lines would bring out some rather more functional abnormality affecting the volume and consistency of different brains, and of the same brain under different circumstances. Marked variations in the resistance of the brain to the leucotome between one patient and another is a phenomenon remarked upon by all neurosurgeons whom the writers have interrogated.

It is even more difficult to assess with any degree of accuracy the significance of those numerous other somatic manifestations in schizophrenia and other functional psychoses such as those which have recently been reviewed and in part re-examined by Shattock. They include small heart and blood vessels, low blood pressure, reduced blood volume, acrocyanosis, capillaroscopic abnormalities, liver damage and gonadal atrophy. Shattock confirmed, in post mortem investigations, Lewis's findings of the small heart and small calibre of limb vessels in all the catatonic subjects in her series of 25 schizophrenics. She observed, in addition, thinness of the auricular wall, which was frequently of the consistency of tissue paper. The capillaroscopic investigations by Olkon (1939) have been continued by a number of workers. Hauptmann (1946) found abnormal capillary patterns in 88 per cent. of patients with a neurotic constitution, and 7 per cent. of his normal control material. In a subsequent contribution the same author and Myerson (1948) reported the findings in 75 schizophrenics and 37 cases of manic-depressive psychosis. In both groups the capillary pattern was abnormal. In the manic-depressive group it was somewhat similar to the findings in the neurotic group, whereas the characteristic pattern in the schizophrenic group (including catatonic and hebephrenic, but not paranoid, patients) was that of immaturity. While Olkon emphasized the permanency of the abnormalities of the nail-bed capillaries, others (Shattock, 1948; and Altschule and Lorenz, 1949) regarded them as being at least partially caused by vasoconstriction, a view which is also suggested

by the similarity of the abnormal capillary structure in schizophrenics to that seen in Raynaud's disease (Davis, 1946) and neurocirculatory asthenia (Cobb, Cohen and Badal, 1946). Shattock put forward the interesting theory that since vasoconstriction of hands and feet is part of the normal physiological mechanism for conserving body heat, its excessive occurrence in psychotics may be due to their failure to respond to increased bodily requirements by adequate rises in metabolic level.

The pathological anatomy of the liver in acute catatonia has been particularly studied by German workers (Gaupp, quoted from Winkler, 1948). It is unlikely that the changes reported (central lobular degeneration and thrombi in the central veins) have any general or primary significance. Kluge (quoted from the same source) regards them as terminal and possibly due to starvation, an interesting hypothesis, in view of the recent deficiency theories of liver necrosis and cirrhosis (Himsworth and Glynn, 1944). Shattock also discussed the possibility of vasoconstriction causing the degeneration in the liver. A liver disturbance was also suggested by De Jong (1945) as an important cause of catatonia.

Perhaps the most interesting individual histological contribution to the problem of schizophrenia is the confirmation by Hemphill, Reiss and Taylor (1944) and Hemphill (1944) of Mott's old findings of atrophy of the testes in schizophrenics by means of testicular biopsies. According to these authors, the histological appearances in the biopsy specimens were similar to those described by Mott, and were not in proportion to the age or physical state of the patient or to the duration of the psychosis. The testes appeared to be damaged most severely in cases where symptoms had developed soon after puberty, and in rapidly dementing and deteriorated chronic patients, least in cases where the onset dated from their late twenties and in paranoid and mild chronic patients. "The pathological picture resembled in certain respects the secondary atrophy caused by hypophysectomy in animals, which may suggest pituitary disorder in schizophrenia antedating the histological and presumably mental pathology." This pituitary disturbance, of course, need not be primary, but may again depend on a disturbance of higher neural control centres.

It is fairly certain that none of these anatomical changes has a convincing claim to being a substrate of the psychoses. Some of them, like the liver change, are very probably secondary phenomena; others, it has been suggested, may be primarily associated with the leptosomic body build and thus be parallel manifestations of common origin with the psychosis. Many of them are examples of the hypo-reactivity and "physiological withdrawal" which Hoskins and his associates observed in psychotics, particularly schizophrenics, when studying their response to stimuli such as thyroid, oxygen, vestibular stimulation, anaphylactic shock, insulin, adrenaline, high and low temperature, glucose intake, etc. (For references see Hoskins, 1946.) This broad biological concept, which has not been without precursors (Hoskins himself quotes Golla's finding of the reduced reaction of psychotics to carbon dioxide), is proving to be the most useful approach yet suggested to the pathology of the functional psychoses. It not only offers explanation for many of the anatomical abnormalities discussed above, but also throws light on metabolic disturbances

such as the nitrogen retention discovered by Gjessing in periodic catatonias, and the stability in schizophrenia of the electroencephalogram under stress, to which Hill and his associates (1949) have drawn attention.

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PHYSICAL THERAPIES.

The flood of experimental and clinico-pathological observations on *convulsion therapy* has subsided during the period under review. The evidence for and against brain damage during insulin and convulsion shock therapy was reviewed succinctly in 1945 by Lewis. The effects of electro-convulsive therapy (E.C.T.) alone were reviewed in 1946 by Alpers, and more recently and indirectly by Karliner (1948), in a treatise on neurological sequelae. The general conclusion from experimental work on monkeys (Lewis; Ferraro *et al.*, 1946), dogs (Lidbeck, 1944) and cats (Alexander and Loewenbach, 1944; Winkelman and Moore, 1944; Winkler and Frank, 1948) is that currents comparable to those used in clinical therapy produce no significant permanent structural change beyond some ischaemic nerve cell changes near the site of the electrodes, and perhaps some diffuse reversible cell and water changes elsewhere. In the case of a patient who died within 40 minutes of his first electrical convulsion, Meyer and Teare (1945) found diffuse cerebral fat embolism without any clue as to its true source, although the patient complained of pain in the back after the fit.

Karliner pointed out that "in the relatively few human brains as yet examined after E.C.T., complicating factors were present in most to blur the

pattern or cast doubt on their significance." Will, Rehfel and Neumann (1948) came to essentially the same conclusion from their review of 33 cases in the literature of death after electro-convulsive therapy.

Equally negative morphological findings have been reported from observations on the brain after experimental *electronarcosis* (Globus *et al.*, 1943). In a human fatality, Alpers and Madow (1948) reported diffuse recent haemorrhages, but this was obviously an exceptional reaction since it occurred during the first treatment, and the patient survived only three hours. The present authors have investigated two cases where death occurred during the fourth and fifth treatment respectively. Histological investigation, including full serial sections of the basal ganglia and thalami, and representative levels of the medulla, revealed no structural change of significance.

On the chemical side, on the other hand, Cerletti (1947) has reported evidence of the presence of a substance, which he calls "acroagonine," produced in the brains of pigs subjected to a series of electro-shocks. Courses of 10-20 intramuscular injections of emulsion of these pigs' brains, into depressed and manic patients, were followed by a favourable clinical response in many, affecting mainly diencephalic neuro-vegetative phenomena.

The histopathology of the central nervous system after fatal *hypoglycaemia* has been reviewed again by Hoff, Grenell and Fulton (1945), and by Spencer (1948). The former workers compared the findings with those in anoxic conditions and emphasized the similarity of the pathological changes in the two types of condition. The present writers, as mentioned in the section on Anoxia, have reviewed nine personal cases, and all the adequately investigated cases in the literature, and have been impressed by the significant divergencies of vulnerability in different parts of the brain, as between hypoglycaemic and anoxic conditions. Whether these differences might be explained in terms of glycogen reserve in the various parts (cf. Chesler and Himwich, 1944), or calls for explanation in terms of specific enzyme systems, remains to be seen.

Neuropathological aspects of *leucotomy* (see the section on Localization of Function for discussion of clinico-morphological aspects) have been touched upon only incidentally in the clinico-pathological and anatomical studies published by the present writers and their associates. From their series now of 122 leucotomized brains, McLardy (unpublished, cf. McLardy, 1948) has determined that the scar usually becomes a granular-walled pigmented cyst in about 6 months' time, and smooth-walled and often unpigmented in about 18 months. By this latter time the cyst has often reached an antero-posterior length of 3 to 4 cm., in the average cut, and the prefrontal region of the frontal lobes shows, externally, a moderate symmetrical reduction in bulk, the anterior horn of the lateral ventricles a moderate compensatory dilatation. Less frequently, and irrespective of the age of the patient or the type of psychosis, only a fibrosed linear slit is found, implying, presumably, that the massive degeneration of fibres on both sides of the cut, instead of resulting in a cyst, has determined a collapse of the surrounding white matter to fill the gap. All lesions probably fill with blood in the first instance, but after 6 months the content of the cyst is a colourless liquid, indistinguishable in naked eye appearance from cerebrospinal fluid, and haemosiderin is confined to a marginal layer

of compound granular corpuscles. Lesions which have involved the anterior horn of the lateral ventricle become sealed off from it by glial scar tissue. *Fatal haemorrhage* was as often (13 cases) due to the cutting, by the leucotome, of a branch of the middle cerebral artery, as of the anterior cerebral artery (12 cases), and could very seldom be attributed to a diseased condition of the arteries. In two cases (one a transorbital leucotomy) damage to the lenticulo-striate arteries had caused fatal haemorrhage. The haemorrhage may rupture into tissue beyond the cut, even in non-fatal cases, thus enlarging the wound to an extent which cannot readily be determined before autopsy. Abscess formation was a rare occurrence; likewise cerebral softening remote from the primary lesion. Cortical cells damaged at the entry mark or elsewhere often showed the ferruginous type of degeneration, but so far no obvious peculiarity has been observed in cases where post-operative epilepsy occurred. The secondary changes in nerve cells of the thalamus take the form of primary irritation which reaches its maximum in the dorsomedial nucleus in about four weeks, in the anterior nucleus in about six weeks and goes on to either recovery or complete degeneration about four and eight weeks later, respectively. The degree of compensatory gliosis appears to be roughly proportional to the rate of nerve cell degeneration. Practically no such primary irritation of nerve cells or subsequent degeneration and gliosis is found in the cortex rostral to the cut. Where significant bilateral damage has been caused to the striatum, Area 13 of the posterior orbital region or the premotor region, *delayed operative death* ensues almost without fail within five months. Where one side only is so affected there appears to be a liability to death significantly earlier (within about 18 months of operation, on the average) than when these structures are spared bilaterally. In the case of haemorrhage the immediate cause of death appears usually to be cerebellar cone formation with medullary ischaemia; in the case of posterior cuts with "delayed death," presumably an inadequacy in various homeostatic mechanisms. Both forms of fatality must be attributed in large part to the *blindness of the operation* (as routinely performed in this country), permitting no satisfactory check on the brain's position in relation to skull markings, its consistency, or its degree of movement with the leucotome.

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THE NEUROPATHOLOGY OF OLIGOPHRENIA.

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THE scope of this review has been limited to neuropathological conditions arising in early life which are commonly associated with certifiable mental defect. Thus most of the prenatal malformations to be listed are those sufficiently benign to permit the survival of the affected individual, at any rate for some years, while the diseases of post-natal origin have been restricted to conditions known to have chronic cerebral sequelae likely to affect intelligence adversely. However, the writer of this article makes no apology in departing on occasion from this programme in the case of certain conditions which seem to him to have a peculiar interest to students of structural aberration. Brief reference has also been made to pathological changes in structures other than those of the nervous system when such features are of relevance to the subject of mental deficiency. On the whole, the years under review have yielded a rich harvest, though so far as this country is concerned the pathology of oligophrenia is as yet in the main an untilled field.

PRENATAL MALFORMATIONS.

Cranial anomalies.—Josephy (1945a) has classified these malformations into two main groups, the craniostenoses, in which the sutures have prematurely closed, and the secondary skull anomalies, which are conditioned by the retarded or perverted growth of the brain. He lists three types of micrencephaly: miniature or "nanencephalic" brains, small brains associated with marked malformation, that is, "malformative micrencephaly," and lastly, brains the small size of which is due to gross destruction, the "destructive" type of micrencephaly. Premature closure of the cranial sutures is dealt with in more detail in an informative paper by Simmons and Peyton (1947), who point out that surgical intervention is necessary if an attempt is to be made to avert the usual mental defect caused by the premature cessation of skull growth. Complete and early premature synostosis leads to the skull anomalies of oxycephaly, the craniofacial dysostosis of Crouzon and acrocephalosyndactylism. Incomplete early synostosis of certain sutures leads to scaphocephaly, brachycephaly, plagiocephaly or to mixed forms. Operative treatment must be started as soon as possible, since after the age of three years there is only a slight increase in intracranial capacity. The authors describe in five cases the results of linear craniectomy, using tantalum foil to prevent the bridging over of the gaps by new bone. The relation of the brain changes to those of the skull in Crouzon's and similar diseases have also been discussed by Eshbaugh (1948). Twenty-five cases that have come to autopsy are

reviewed, and the author adds one of her own in which a local constriction of the skull had apparently led to slight hydrocephalus. Although in most cases the cerebral changes are due to the retarded skull growth, it is clear that a number of coincidental developmental anomalies of the brain may be found associated with these malformations of the cranium. This is exemplified in a case by Lhermitte, Ajuriaguerra and Trotot (1944), in which the brain of a twenty-months-old infant with oxcephaly showed agenesis of the posterior part of the corpus callosum and of the inferior vermis of the cerebellum in addition to general atrophy of the cerebral cortex.

Congenital hemihypertrophy, a condition often associated with mental defect, is reviewed by Ward and Lerner (1947). They recorded the autopsy findings in an eight-months-old infant, and found no abnormality in the nervous system or pituitary apart from a brain weight of 1,375 gm. Rugel's (1946) case was that of a two-year-old infant with right-sided hemihypertrophy whose head appeared hydrocephalic. A large hemangioma covered most of the left arm and left side of the lip. The adrenals and ovaries were symmetrically developed, but in the case of the other paired organs those of the right side were the heavier. The brain was large, weighing 1,670 gm., and the right cerebral and cerebellar hemispheres were relatively increased in size.

Agenesis of the corpus callosum and associated malformations are the subject of an important paper by Kirschbaum (1947). Complete absence of the corpus callosum was found in two mental defectives. In the first case pluriglandular and other developmental changes (megacolon, Paget's disease of bone, etc.) were present. The convolutional pattern showed abnormalities which were a direct consequence of the absence of corpus callosum, namely, radially converging gyri on the medial surfaces of the brain. A noteworthy feature was the presence of well-developed aberrant callosal bundles running in a longitudinal direction on each side of the brain, instead of passing transversely between the two hemispheres in the form of a normal corpus callosum. In the second case (in which death occurred at the advanced age of 84 years) these longitudinal bundles were absent, having presumably been prevented from growing because of masses of heterotopic nerve cells that lined the walls of the lateral ventricles. Bilateral occipital porencephalies, microgyria and a small meningioma attached to the caudate nucleus were other peculiar features. The possibility that maternal rubella may lead to agenesis of the corpus callosum in the foetus is suggested by the case of a thirteen-months-old infant examined in detail by Friedman and Cohen (1947). The mother had had a transient rash on the legs during the second month of pregnancy. In addition to absence of the corpus callosum, anterior commissure and pyramidal tracts, there was a mild diffuse subcortical sclerosis and secondary hydrocephalus. Bilateral posterior cortical cataracts, scarring of the kidneys and fibrosis of pancreas and thyroid completed a complex pathological picture.

The corpus callosum was absent in an example of *congenital agyria* recorded by Josephy (1944). The brain of this nine-months-old infant was found to weigh only 300 gm., and was smooth apart from the Sylvian fissure, the three temporal gyri and a few rudimentary sulci in the occipital and frontal lobes. The characteristic narrow band of myelinated fibres which is found in such

brains lying immediately below the grey matter of the cerebral cortex is considered by the author to be composed of fibres that have been prevented from reaching the centrum semiovale by the mass of neuroblasts in the persistent intermediate layer. This explanation differs from the theory put forward many years ago by Bielschowsky, in which the strand of fibres is regarded as being homologous with the normal subcortical arcuate or U fibres. A more severe malformation is exemplified in the interesting case of cyclocephalon described by Aranovich (1943). This infant, who survived only seven days, exhibited microphthalmos and multiple chondromata of the face. The lissencephalic hemispheres formed the boundaries of a common ventricle. Arhinencephaly was present and there was no corpus callosum, while the olives, red nuclei and hypothalamus were hypertrophied.

According to Marburg and Warner (1946), the causative factor in cyclopia and arhinencephaly is a disturbance at the base of the forebrain and interbrain occurring in the first four weeks of development whereby the meninges are changed into a fibrous mass leading to the destruction of the olfactory bulbs, tracts and striae and part of the optic chiasma. In Marburg's case a thick connective-tissue membrane covered the floor of the third ventricle as far as the infundibulum. The little known relationship between defects of the olfactory brain and genital malformation is the subject of a paper by Gruenfelder and Lasch (1945). A man of eunuchoid physique, aged 34 years at death, exhibited hypoplasia of penis, scrotum, testes and prostate, the right kidney and ureter being absent. In the brain the left olfactory tract was absent and the right tract stunted. The authors have collected twelve other cases from the literature in which hypoplasia or aplasia of the olfactory nerves were associated with anomalies of the genital organs.

Two varieties of *cerebellar malformation* have been described by Lichtenstein (1943a), the first case exemplifying simple hypoplasia of one cerebellar hemisphere the microscopical structure of which was normal, the second case being one of aplasia of the vermis associated with a small and in part microgyric left cerebellar hemisphere. Secondary (transneuronal) degeneration of the olives and ipsilateral dentate nucleus had also taken place. Hypoplasia of the cerebellar vermis in combination with dilatation of the fourth ventricle and cisternal arachnoid cyst has been recorded by Shryock and Alexander (1943). It is suggested that the condition follows delay in the opening of the foramina of Luschka and Magendie at about the fourth month of foetal life. Absence of cerebellar vermis with gross dilatation of the fourth ventricle was also a feature of the complicated case described by Sidenberg, Kessler and Wolpaw (1946). The anterior half of the corpus callosum, the anterior horn of the right lateral ventricle and also the olfactory bulbs and tracts had failed to develop. There was an oval defect 1 cm. in diameter in the floor of the third ventricle. Fallot's tetralogy was present and death was brought about by a cerebral abscess—a common complication of this type of cardiac defect (Hand, 1947). Under the title "Agenesis of the White Matter with Idiocy," Waggoner, Lowenberg-Scharenberg and Schilling (1942) have described an unusual pathological form of familial low-grade mental deficiency. Examination of one adult case showed a small brain with absence of myelin throughout

much of the cerebral hemispheres. The white matter was affected by wide-spread gliosis, and in the cerebral cortex the nerve cells were disorientated and reduced in numbers. Benda (1948) has separated from the main mass of low-grade defectives a relatively homogeneous group characterized by dolichocephaly and by stigmata of bodily maldevelopment, such as asymmetry of limbs, spinal curvature and spina bifida. The brain and spinal cord exhibit minor malformations, hypoplasia, defective myelination, small heterotopic collections of nerve cells, and slight irregularities of nerve cell arrangement in cerebral and cerebellar cortices and also in the grey matter of the spinal cord.

Porencephaly.—Yakovlev and Wadsworth (1946a), in an important contribution, have described two cases showing symmetrical congenital clefts in the cerebral mantle arising as the consequence of a failure of growth and differentiation of circumscribed areas of the cerebral wall during the first two months of foetal life. Such clefts are characterized by absolute symmetry and orientation in the axis of an individual sulcus or fissure. Richly cellular grey matter persists in their walls, and the marginal layers of the cortex covering the lips of these clefts are fused into a solid cellular seam ("the pia-ependymal seam"), which is continuous with the ependyma, subependymal cell plate of the underlying ventricle or with the corpus striatum. Myelinated fibres may be found within the seam, and there is no glial or connective-tissue scar as in "encephaloclastic" porencephaly. Internal hydrocephalus is lacking, but the occipital horns of the lateral ventricles may be relatively large ("colpocephaly"). In a later paper (1946b) these authors described three specimens in which the lips of the clefts had become separated on account of the stretching of the cerebral walls by internal hydrocephalus. Large gaps are thus formed in the cerebral cortex by a process quite distinct from that of encephalomalacia. There is a close similarity between the histological structure of the pia-ependymal seam in the closed parts of the cleft and that of the pia-ependymal ridges of attachment of the roofing membrane along the borders of the gaps. That such clefts are not always bilateral is suggested by a case of congenital hemiplegia reported by Papez and Vonderahe (1947). In a boy, aged $2\frac{1}{2}$, a deep agenetic cleft bordered by microgyria occupied the sensori-motor and insular regions, sparing area 6 and the upper part of area 4. This lesion had led to a flaccid type of hemiplegia reminiscent of the condition described by Tower following pyramidal section in apes.

A form of porencephaly similar to that described by Yakovlev and Wadsworth (1946b) is reported by Cohn and Neumann (1946). In this case the brain weighed only 240 gm. and gross symmetrical defects occurred in the frontal and parietal areas, so that transillumination of the skull was actually possible. The authors point out that despite the symmetry of the lesions and the microgyria present in the edges of the porus no "pia-ependymal seam" was found, and they claim that in certain cases it is futile to argue whether vascular or agenetic processes are to be held responsible for these prenatal porencephalies. Davison and Friedman (1946) have described an unusual form of cortical defect, presumably of developmental origin, which consisted in a large depression that replaced the anterior part of the temporal lobe and third frontal gyrus, thus exposing the Island of Reil. This cavity

was covered by arachnoid, and its walls showed no sign of compression or destructive process.

TUBEROSE SCLEROSIS.

An informative paper by Moolten (1942) gives an admirable review of the varied features of what he prefers to call the "tuberose sclerosis complex." Evidence is cited which "enables one to make a special case for the high incidence of cerebral neoplasm in tuberose sclerosis without doing violence to the concept that the underlying basis for the disease is a disseminated tissue malformation (hamartosis)." Defective organization in the embryonic brain is carried into mature existence in the form of unrealized cell potencies for differentiation and of refractoriness to local and neurotropic organizer influences.

The *bony changes* which may be found in association with tuberose sclerosis have been described in detail by Hall (1943). In one of his cases "melorheostosis" was present in the form of an extensive and irregular hyperostosis, most marked in the bones of the forefinger and first phalanx of the thumb. The X-ray picture has been likened to the "guttering of a candle"—a remarkable echo of the simile often employed to describe the paraventricular tumours seen in the brain in this disease. Hall believes the condition is due to a local defect in the periosteum, which allows a spread of ossification from the affected bone into the adjacent tissues. Cyst-like rarefactions in the bones of the hands was a feature recorded by Samuelsen (1942), his case also showing X-ray appearances of the lungs resembling those of Boeck's sarcoid. At autopsy a cystic lung with numerous small air-distended cavities was found, histological examination revealing small patches with thickened alveolar septa and pigment accumulations. Dunsdale (1946) has described a case of tuberose sclerosis showing hyperostosis frontalis interna as well as periosteal thickening and areas of rarefaction in the metacarpals and metatarsals. According to Dickerson (1945), a characteristic roentgenographic change in tuberose sclerosis is the finding of zones of increased density in the calvaria—a change which seems in some way related to puberty. This hyperostosis affects not only the inner table but also the diploic trabeculae, and often seems to overlies directly the glial nodules of the cortex. Abnormal hypothalamic activity was suggested by Balo (1944) as the cause of the bony changes in his case, which showed the unusual association of multiple chondromata of the upper thigh with a cyst in the posterior lobe of the pituitary.

Malignant transformation of the tuberose nodules in the brain has been recorded by Fattovich (1947), Pratt-Thomas (1947) and Thiebaut, Fénelon and Berdet (1947). In all these instances the histological appearances of the growths were those of a spongioblastoma. The cardiac tumours often found in cases of tuberose sclerosis have been well described by Batchelor and Mann (1945), who consider that they should be termed "congenital nodular glycogen tumours of the heart" rather than rhabdomyomata. The kidney tumours that are also a common feature of this disease have received special attention in an article by Rezza (1946). Ross and Dickerson (1943), whose survey of the clinical features of 25 cases contains many valuable observations, have described the post-mortem findings in three cases. One of these showed a

peculiar enlargement of the cisterna magna caused by a deep concavity between the brain stem and a small cerebellum, the inferior surface of which was sclerosed. An unusual feature was the presence of extensive gliosis and atypical glial cells in the optic tracts. This article is specially informative in giving details of the pathological changes found in the eyes in cases of tuberose sclerosis. These ocular manifestations have also been well described by Hall (1946), whose case includes an account of the histological appearances of the retinal phakomata.

CONGENITAL VASCULAR ANOMALIES.

A comprehensive review of intracranial vascular tumours and malformations has been provided by Noran (1945), under the title "Progressive Multi-form Angiosis." Arieti and Gray (1944) have described the case of a youth of 17 who developed epileptic attacks, and whose mentality and behaviour suffered progressive deterioration. At post-mortem an arteriovenous angioma of the left parietal lobe was found and, in addition, large aneurysms of the circle of Willis and abdominal aorta. Divry and Van Bogaert (1946) report a familial disorder restricted to males which was characterized by slowly progressive dementia with epilepsy and signs of pyramidal and extrapyramidal motor involvement. The leptomeninges and, to a lesser extent, the brain itself were the seat of capillary and venous angiomata which showed no calcification. Small areas of necrosis were seen in the cerebral cortex, while extensive demyelination of the white matter accompanied by dense gliosis and prelipoid degeneration products were unusual features of these cases. The authors believe that this diffuse loss of myelin is not to be related directly to the vascular anomaly, but is rather an additional expression of a more generalized tissue dysplasia.

There have been several recorded instances of the Sturge-Weber syndrome. In a case reported by Haemerlinck, Myle and Van Bogaert (1947) the dura mater was bilaterally implicated by an angioma. Although X-rays had shown no calcification, histological examination revealed abundant fine precipitations in the cortex. This case also exhibited advanced atrophy of the white matter of the affected hemisphere. According to Lichtenstein and Rosenberg (1947), who describe an example of occipital lobe meningeal angioma with underlying atrophy of the brain, the brain changes of Sturge's disease "are exclusively the result of excessive vascularization of the overlying leptomeninges, producing venous and capillary stasis of the cerebral cortex." Green (1945) gives an account of a three-year-old boy from whom a haemangioma of the left parietal lobe was surgically removed. The upper layers of the cortex showed characteristic calcification, which in the author's opinion represented calcareous degeneration of primary angiomas. Bentzen (1947) describes two patients with Sturge's disease in whom occipital lobectomy stopped the fits. He remarks that in 65 out of the 72 cases he was able to find in the literature calcification of the pial angiomas had taken place, while in 33 cases these angiomas were limited to the occipital lobe. The significant feature in Rorvik's patient was the ophthalmoscopic finding of a deep conical excavation in the central part of the optic papilla, around the edge of which abnormally numerous

blood vessels were visible. Furtado and Rodrigues' (1947) patient was an oligophrenic girl, who exhibited athetosis of the paretic arm, intermittent diabetes insipidus and obesity with polyphagia in addition to the usual features of Sturge's syndrome. In a discussion of the pathogenesis of the brain calcification, which in this case involved almost the whole occipital lobe, the authors point out that the calcification is originally perivascular and leads later to thrombosis and eventual disappearance of the vessels, so that it is only in young patients that it is possible to trace by arteriography a connection between blood vessels and the calcareous deposits. Calcification involving both sides of the brain and naevi affecting both sides of the face and body were features of a mentally defective child described by Worster-Drought (1948). Burke (1948) has also reported a case in which a central naevus above the nose was associated with bilateral cerebral calcifications later confirmed at post-mortem.

HYDROCEPHALUS.

The condition of *congenital atresia of the foramina of Luschka and Majendie* is exemplified in three cases reported in detail by Taggart and Walker (1942). If the foraminal atresia occurs at about the fourth month of foetal life the great dilatation of the fourth ventricle prevents the development of the posterior part of the cerebellar vermis. If, on the other hand, the opening of the foramina is only delayed, the fourth ventricle is still dilated, but the hydrocephalus is not progressive. Nevertheless, even this transient increase of intracranial pressure seems to interfere with the normal development of the cerebral cortex and mental deficiency results. Another example of this condition has been recorded by Walker (1944). A twenty-year-old woman who had always had a large head and unsteady gait suffered from headaches and fainting attacks. X-rays showed the typical appearances associated with atresia of the foramina of the fourth ventricle, namely, an enormously enlarged posterior fossa and conspicuous elevation of the lateral sinus.

Atresia and stenosis of the Sylvian aqueduct is the subject of a paper by Globus and Bergman (1946), who have reviewed 23 cases and have added 3 of their own. In about half the cases symptoms of obstruction appeared before the age of one year. The most likely cause is considered to be glial overgrowth and protrusion into the aqueduct, the ependymal lining of which is defectively developed. Hydrocephalus was the only clinical feature in a mentally subnormal youth of eighteen who was found at autopsy to be suffering from an *arteriovenous aneurysm of the great vein of Galen* (Alpers and Forster, 1945). The arterial supply came from the posterior cerebral and choroidal arteries. It is suggested that hydrocephalus (which was a feature of the three previously recorded cases) was caused by the pressure of the aneurysm upon the aqueduct. Another rare cause of congenital hydrocephalus is lipoma of the quadrigeminal plate, an example of which has been reported by Davison (1945).

The Arnold-Chiari deformity has been the subject of several communications. Ogryzlo (1942) described seven cases, three being adults, upon whom operation was performed. The simplest variant of the deformity (type 1 of

Chiari) shows elongation of the tonsils and medial parts of the inferior cerebellar lobes in the form of a tongue-like projection enveloping the medulla and passing downwards into the cervical vertebral canal. A more common variant (type 2) shows in addition downward elongation of medulla, pons and sometimes midbrain, the fourth ventricle thus extending below the level of the foramen magnum. Dense adhesions often involve the herniated parts. Spina bifida and myelomeningocele are present and hydromyelia and doubling of the central canal may occur. The deformity is caused by fixation of the spinal cord at the site of the spina bifida, and this leads to traction upon brain stem and cerebellum as bodily growth proceeds. True syringomyelia and syringomyelia-like conditions due to pressure upon the cervical cord and interference with its blood supply may be found not only in association with the Arnold-Chiari deformity, but also with platybasia and the Klippel-Feil deformity (Lichtenstein, 1943). Craniolacunia was frequently seen in Ingraham and Scott's (1943) series of 20 cases. In Shryock's (1944) eleven-month-old infant the deformity was associated with complete closure of the aqueduct, as in Lichtenstein's (1942) cases. The Arnold-Chiari deformity is usually seen in conjunction with spina bifida or platybasia, but in Bucy and Lichtenstein's (1946) adult case no obvious cause was found. The symptoms were referable to increased intracranial tension, and to compression of the lower cranial nerves, brain stem, spinal cord or cerebellum.

Yakovlev (1947) has given a valuable classification of the clinical forms of paraplegia which are associated with hydrocephalus: The flaccid type, in which incontinence occurs and the legs are anaesthetic because of lumbosacral cord anomalies, the spastic type in which the primary lesions are purely cerebral, and a rarer mixed type. The anatomical explanation as to why spastic paresis generally affects only the legs of hydrocephalics seems to be that those fibres of the pyramidal tracts which originate in the paracentral lobules and the upper part motor cortex become selectively stretched as they skirt the enlarged lateral ventricle *en route* for the posterior limb of the internal capsule. Benda (1947a) found 11 cases of hydrocephalus in 200 autopsies on institutional defectives. He believes that hydrocephalus may result from pathological changes in the ependyma, which interfere with the exchanges between brain tissue and spinal fluid.

A grossly enlarged head of egg-like contour may signify the presence of *hydranencephaly*, as in two cases described by Watson (1944). The infants were full term, and seemed little if at all different from normal babies; yet the cerebral cortices of both were almost non-existent, being represented by a thin membrane underlying the leptomeninges. This condition seems to be due to a resorption of the previously formed cerebral hemispheres which takes place rather late in foetal life and it is not, therefore, to be regarded as the consequence of agenesis. The reader is also referred to a very full account of the subject of hydroencephaly by Lange-Cosack (1944).

MONGOLISM.

Benda's (1947c) book on mongolism and cretinism gives an invaluable summary of the physical, endocrine, nervous and psychological features of

these conditions. In mongol infants dying below the age of two years the brain growth is retarded, myelination is poor, and perivascular loss of nerve cells and myelin is commonly seen. Benda believes that oedema of nerve cells is a significant pathological feature in mongol brains, and states that the histology of the central nervous system "indicates circulatory deficiency, asphyxiation, oedema and brain swelling"—factors producing widespread disease of the nerve cells which eventually leads to "general atrophy and sclerosis." In older patients the brain shape closely follows the characteristic skull contour with steep occiput, short frontal lobes and distorted temporal gyri. The gyri of the convexity seem broad and simple, but hide in their depths submerged sulci which may show the typical mongolian abnormality of fusion of their margins. The cortical nerve cells are more densely packed than in normal brains, their smallness of size being due to "stunting through degeneration." Patchy loss of nerve cells is recognizable in every case, and "is due to a continuous oedematous submerging of nerve tissue in which cell after cell meets death by suffocation." This conception of a progressive nervous degeneration in mongolism is a distinct novelty. Benda also describes in detail the frequently encountered minor malformations of the spinal cords of mongols. Of special interest is the section on endocrine pathology, two types of pituitary abnormality being encountered. In the first there is a "deficiency of the gamma cell system and general inability of formation of chromophilic elements." In the second there is a chromophilic shift towards eosinophilia with absence or deficiency of the gamma cells and pathological changes in the beta cells.

Prassoli (1948), who also has reviewed the endocrine pathology in this disease and has added a description of the findings in a six-months-old mongol, considers hypoplasia of thyroid, thymus and parathyroids to be the most significant changes. Fatty infiltration with fibrosis of the liver was frequently seen in mongols by Roosen-Runge (1947), who regards these changes as the consequence of endocrine abnormality. It is interesting to note that identical liver changes are sometimes seen in patients with hydrocephalus or encephalomalacia which have led to infundibular damage.

Ingall's (1947) review of the post-mortem findings in 50 mongols contains an excellent account of the macroscopic pathology of the condition, and he has reported another example of cerebellar and brain stem hypoplasia, a finding not infrequently associated with mongolism. Middle-aged mongols may show premature senility and mental deterioration, and these changes may be reflected in the brain. In a forty-two-year-old mongol Bertrand and Koffas (1946) demonstrated numerous senile plaques, and in three of Jervis's (1948) mongols, who were aged 47, 42 and 37, senile plaques, Alzheimer's neurofibrillary change, pigmentary degeneration of nerve cells, gliosis and deposits of pseudo-calcium were found without evidence of arteriosclerosis.

BIRTH INJURY.

Agnes MacGregor (1946), in an analysis of the causes of 1,053 stillbirths and neonatal deaths, found intracranial haemorrhage in 25 per cent. of cases. Subdural bleedings were relatively commoner in full-term babies, while intra-

ventricular haemorrhage was almost exclusively a feature of the premature. The experimental production of asphyctic cerebral lesions in foetal guinea-pigs forms the subject of an important paper by Windle (1943). Morrison (1946), working with dogs and monkeys, found that repeated exposure to mild hypoxia led to a demyelination of the white matter resembling that of Schilder's disease. An exhaustive review of the various conditions (including asphyxia neonatorum) that may lead to anoxia of the central nervous system has been given by Hoff, Grenell and Fulton (1945). Courville and Marsh (1944), in their comprehensive classification of the late residual effects of asphyxia neonatorum upon the human brain, emphasize the great variety of these late sequelae, which range from gross cerebral or cerebellar atrophy to macroscopically normal brains in which only microscopical search reveals a scattered loss of nerve cells. Benda's (1943, 1945) classification groups birth injuries into three categories: "mantle sclerosis," that is to say, degeneration of the cerebral cortex with necrosis of the subcortical white matter, "cystic degeneration" of the central white matter, which may behave as a progressive disease, and "diffuse patchy devastation." This last condition, which was found in no fewer than 16 out of the 24 cases of birth injury which were pathologically examined, is characterized by scattered areas of nerve cell destruction in the cerebral cortex combined with small necrotic foci in the basal ganglia and the subependymal region, the latter lesions being localized in the drainage area of the great vein of Galen. According to Benda, birth injury is responsible for at least 30 per cent. of idiots, and his (1945) paper is of outstanding interest. Norman (1944) reported in detail three cases in which birth injury seemed to be pathogenetically related to hypermyelinated ulegyria ("atrophic sclerosis"). The frequently observed multiplicity of these small, sclerotic convolutions was considered to be in the nature of a post-natal malformation conditioned by the distorting influence of gliosis arising from necrotic lesions in the vicinity. In a later paper (1947a) the same author has described three examples of *état marbré* of the corpus striatum, in one of which the thalamus was also affected by hypermyelination. Evidence is brought forward to support the view that these lesions are the consequence of anoxia at the time of parturition, and are in no way related to prenatal malformative processes. Massive central porencephaly or cystic degeneration of the central white matter, a condition in which the cerebral hemispheres may be reduced by softening to thin sacs of fluid while the basal ganglia remain relatively intact, is the subject of an informative paper by Marburg and Casamajor (1944), who have described two examples. They regard this form of encephalomalacia as a consequence of phlebotasis or phlebothrombosis initiated by birth injury, although infection or direct injury to the foetus *in utero* may occasionally be responsible. Stevenson and McGowan (1942), however, who reported seven such cases of cerebral cavitation, could come to no clear conclusion as to causation, though they thought that the appearances of some of the brains indicated that the destruction was of pre-natal origin. Three of these infants were syphilitic. There was much to suggest that trauma at birth had occurred in an infant described by Marburg, Rezek and Marks (1945). Delivery had been by forceps, and at birth the baby was found to be bleeding from the ear and exhibited ecchymoses all

over the body. Death took place at the age of ten months, and at post-mortem a large porencephaly of encephaloclastic type was present. The authors claim that arrest of development probably does not cause porencephaly, since the changes often considered to be the consequence of developmental disturbance may be ascribed with greater justification to venous lesions. Similar cyst-like brain softenings in infancy, apparently related to birth injury, were the main features on four cases reported by Christensen and Schondel (1946), who point out that early death is the rule in such conditions. Norman (1948) has given a brief account of the clinical and pathological findings in nine cases of cerebral diplegia attributable to birth injury. The series included both symmetrical and asymmetrical forms of paresis. Kuhn (1948) has presented two cases of birth injury which illustrate the commonly encountered sclerotic and cystic changes in the brain and also the progressive course that may be taken by these lesions. A vascular lesion of the medial nucleus of thalamus which was probably sustained at birth was the only relevant pathological lesion in the interesting case recounted by Engel and Aring (1945). Clinically, this patient suffered from peculiar seizures with features suggestive of hypothalamic disturbance.

Subdural haematoma is a frequent sequel to birth injury, though it also commonly follows trauma to the head in the first six months of life. The great importance of the early recognition of this condition, which is amenable to surgery, is stressed in an admirable paper by Ingraham and Matson (1944). Enlargement of the head in infancy should never be regarded as due to congenital hydrocephalus until bilateral subdural haematoma has been ruled out. Govan and Walsh (1947) have discussed the ocular signs associated with subdural haematoma. Subhyaloid haemorrhage in infants is an almost certain indication of the condition. The frequency of bilateral subdural bleeding in infants is attributed to the lack of the dural and arachnoid adhesions, which in later life give support to the cortical veins at their entry into the sagittal sinus. The undetected presence of the characteristic subdural haemorrhage membrane, which is analogous to that found in association with the chronic pachymeningitis haemorrhagica of adults, is regarded by Fincher (1944) as a possible cause of microcephalus following injury at birth. Enlargement of the head in birth-injured infants may also follow subarachnoid haemorrhage (Babson, 1944).

KERNICTERUS.

While the numerous papers published on this subject in the years under review have added little new to what was already known about the localization of the neuro-pathological changes, much discussion has taken place as to the reason why only a proportion of infants suffering from icterus gravis later develop kernicterus. The condition has not been reproduced in animals, and never occurs when obstructive jaundice is the only factor (Doktor, 1945). Diamond and Denton (1945) pointed out that the severity of the anaemia was of no apparent significance, and thought that the cerebral damage was associated with a high degree of maternal sensitization. Vaughan (1946), in an excellent study of 74 infants with erythroblastosis, found oedema and also a

low birth weight to be commoner in the group of infants suffering from kernicterus. Vaughan also mentions the frequency of pulmonary haemorrhage in cases of kernicterus—a phenomenon which has also been occasionally reported as a consequence of birth trauma. Wiener and Brody (1947), who described the neuropathological changes in one case of kernicterus, suggested that agglutinins are milked into the infant's circulation during labour and produce intracapillary thrombi, the damaged brain subsequently taking up the bile pigments—a theory severely criticized by Levine in the later discussion to the paper. Stiller's (1947) follow-up of 35 erythroblastotic children showed no correlation between brain damage and the degree of jaundice, intensity of the anaemia, the number of transfusions given or the degree of enlargement of liver or spleen. Fannet and Lieberman (1946) put forward the suggestion that kernicterus is likely to occur when the maternal antibodies are produced in high concentration relatively early in pregnancy at a stage when the haemopoietic system of the foetus is unable to compensate for the red cell destruction. There is also the possibility that red cell destruction *per se* is injurious to developing neurones. The evidence put forward by these authors that icterus gravis may give rise to a form of "undifferentiated" mental deficiency without clinical neurological abnormalities has been discounted by Cappell (1947), who points out that although mental deficiency may certainly arise as a result of Rh incompatibility, the damage inflicted upon the cerebral cortex is always found in association with the usual kernicterus of the extrapyramidal motor centres. Cappell (1947) also states that the profound liver damage exhibited by so many cases is absent (so far as histological evidence is concerned) in others. This point is of importance, since Pentschew (1948) has postulated that the damaged liver in cases of kernicterus fails to manufacture a hypothetical substance, "antihypoxydin," which is presumed to be essential to the oxygen metabolism of the brain, especially in the areas selectively affected by icterus, namely, the pallidum, cornu ammonis, striatum, subthalamic body and floor of the fourth ventricle. In another authoritative article Cappell (1948) writes that he is not convinced that the brain lesions occur before birth, and that he has been impressed by the frequency of cases in which there has been difficulty in establishing breathing. It is thus possible that anoxia at birth may be a determining factor. Neuropathological findings in cases of kernicterus are also described in detail in the valuable reviews of Mann and Courville (1948) and of Becher (1948). The latter has confirmed the experience of other investigators in finding no evidence of agglutination thrombi in the capillaries. Nor was proliferation of neuroglia, microglia or connective tissue seen in association with the shrunken, bile-stained and eosinophilic nerve cells of the affected areas. In one of Gilmour's (1944) cases the body of Luys was singled out as the only icteric nucleus. Van Bogaert's (1947a) patient, a girl, aged 6, who exhibited at one stage violent movements of hyperextension, was shown to have atrophy of the bodies of Luys and, to a less extent, of each globus pallidus.

LIPOIDOSES.

In 1942 a special number of the *Journal of the Mount Sinai Hospital* was dedicated to Bernard Sachs, and this appropriately contained several important

contributions to our knowledge of amaurotic idiocy and allied disorders of lipid metabolism. The article by Globus (1942), which contains descriptions of the clinical and pathological features of all the varieties of amaurotic idiocy and adds twelve new infantile cases and one new juvenile case, is probably the most informative and best illustrated review of the subject yet published. An account is given here of the little known changes in the posterior lobe of the pituitary, which shows the characteristic neuronal swelling and lipid storage in the form of globoid bodies. In the same journal Davison's (1942) paper on the effects of a disturbed lipid metabolism upon the central nervous system is also noteworthy. In it he has described a case of infantile amaurotic family idiocy associated with generalized visceral lipoidosis, a case of Gaucher's disease with bony involvement and nerve cell abnormalities in the corpus striatum and spinal cord, and lastly, an example of the Schüller-Christian disease showing in the brain scattered plaques of demyelination and groups of foam cells. The infantile variety of amaurotic idiocy has been found in association with congenital hydronephrosis of a solitary kidney by Lipman *et al.* (1948), and also in conjunction with an abnormality of the marrow of the long bones (Nassau, 1946). In a case reported by Nordlow (1946) the cherry red spot appeared at the age of four months and was the first abnormal sign in a syndrome that took three years to develop. The histological appearances of the retina and optic nerve in Tay-Sach's disease have been fully described by Hassin (1943), and are analogous to those found elsewhere in the brain. Marburg (1944) has studied the endocrine glands in this condition, and has brought forward evidence that the medulla of the adrenal is especially impoverished—a finding to be correlated with the marked asthenia observed in these infants during life. Changes were also seen in testes, ovaries and thymus. Marburg (1943) has also drawn attention to the presence of nerve cell inclusion bodies in the infantile form of the disease—a finding usually associated with myoclonic states. Inclusion bodies "in vast numbers" were also present in an example of the late infantile form described by Hassin (1943). This infant exhibited severe and continuous clonic contractions of eyelids and legs. A peculiar feature of the otherwise typical juvenile case of Lubin and Marburg (1943) was that despite frequent seizures the electroencephalogram was within normal limits. In the brain there was little if any loss of myelin—a finding to be correlated with the small amount of nuclear damage in the nerve cells. Athetosis and torsion spasm were the main clinical features of a dystonic syndrome described by Marques (1947). This case was proved histologically to belong to the category of juvenile amaurotic family idiocy, although there was no optic atrophy or retinal anomaly. Marques (1942) has also reported another example of the disease which was associated with spina bifida. Winkelman (1946) has described an example of the much rarer adult variety. This was a man dying at the age of twenty-five in whom fits had started eight years previously. Cells typical of amaurotic idiocy were seen singly, or in groups, throughout the brain, with especial frequency in the cornua ammonis and subthalamic nuclei. The bodily organs were unaffected by lipoidosis. In a family investigated by Lubin, Marburg and Tamaki (1943) a progressive flaccid paralysis associated with squint, dysphagia and mental impairment affected

three siblings and proved fatal by the age of two years. In one infant a clinical diagnosis of Werdnig-Hoffman disease was made, but histological examination showed nerve-cell changes resembling those of infantile amaurotic idiocy, though the cells were not so distended as is usual in the latter disease. Pre-lipoid granules were found in nerve cells of spinal cord, brain stem and cerebellum, to a less extent in the deeper layers of the cortex, and also in spleen, liver, lungs, heart and thymus. The pyramidal tracts and part of the posterior columns were deficient in myelin.

Jervis (1942) has drawn attention to a familial disorder having many pathological features in common with juvenile amaurotic idiocy, while clinically it was characterized by severe mental defect and dwarfism due mainly to the stunting of the leg bones. Most of the distinguishing signs of the Hunter-Hurler syndrome (gargoylism) were absent, as also was amaurosis. A characteristic facies, a thick skull giving a peculiar spongy X-ray appearance, and broad short hands with incurving of the little finger were features of the syndrome. Chemical analysis of the brain by Sperry (1942) gave very similar results to those obtained by Klenk (1939) in the ordinary juvenile form of amaurotic idiocy.

A condition having a much closer resemblance to gargoylism is the so-called Typus E of de Lange and Woltring (1946). There is in this syndrome, however, no corneal clouding, kyphosis or enlargement of the sella turcica, and mental deficiency and peripheral deafness are present. De Lange, Gerlings, de Kleijn and Lettinga (1943) have now described the post-mortem findings in one of these children. The brain examination was entirely negative as regards lipid storage. The enlarged liver showed mild cirrhosis and gross accumulation of glycogen. The heart valves showed sclerotic thickening, and mucoid degeneration of connective tissue was found in different parts of the body. De Lange (1942) has also reported upon a typical case of *gargoylism*. The nerve cells showed the changes of juvenile amaurotic idiocy in varying degree. The frontal and central parts of the cortex were most severely affected; olives, pons and occipital cortex suffered least, while the nerve cells of the striatum and pallidum occupied an intermediate position as regards severity of damage. The liver showed early cirrhosis and vacuolization of its cells. Kny's (1942) case was also clinically and radiologically typical. The liver showed cirrhosis, and its cells contained lipid granules that stained red with Sudan III. The nerve-cell changes were marked in frontal cortex, thalamus, brain stem, reticular part of the substantia nigra and spinal cord, the lipid inclusions staining a faint red with Scharlach R and Sudan. An account of the pathology of Hurler's disease has also been given by Sear and Maddox (1945), though their infant was described only from the clinical standpoint. In this case the parents were consanguineous. An elaborate review of the literature and the detailed pathological examination of a new case makes Lotte Strauss's (1948) paper particularly valuable. Up to the present 119 gargoyles have been reported and only 16 have come to autopsy. This case showed internal hydrocephalus due to bony deformities causing compression of the mid-brain. (Grüneberg (1943) found a similar condition in mice.) Distension of nerve cells with a substance staining deeply with Sudan III was most evident in the cells of

the cerebral cortex and anterior horns of the spinal cord, and there was a moderate degree of associated gliosis. In addition to lesions of brain, eyes, skeleton and viscera which have been previously described by others, a very striking generalized alteration in the connective tissue of the body was reported, namely, the presence of large vacuolated cells (probably fibroblasts), which were found in association with collagen overgrowth. The cerebral pathology of the infantile form of *Gaucher's disease* has recently been described by Schairer (1948). Storage of "lipoid" was widespread throughout the brain, being maximal within the nerve cells of the dentate nuclei.

DIFFUSE PROGRESSIVE LEUCOENCEPHALOPATHY.

The early infantile form of "diffuse sclerosis" of the brain, first described by Krabbe, was found in two cases reported by Jervis (1942*b*). The condition is a rarity, only 12 other cases having been reported, and from an analysis of these a characteristic clinical syndrome emerges, in which tonic fits are an important feature. Numerous large pale glial nuclei of a type normally seen in the later stages of foetal development were found in the cerebral cortex and basal ganglia. Jervis considers that the presence of these immature elements gives support to the theory that the defective metabolism of myelin seen in this condition has been brought about by a primary abnormality in the neuroglial cells.

De Lange (1946) has provided a detailed study of the subacute familial type of diffuse sclerosis which is associated with the name of Scholz. In this case the patient was found to be feeble-minded at the age of five years. She became ataxic and started to deteriorate from the age of twelve, when fits were first observed, death occurring in status three years later. There was widespread myelin and axis cylinder loss in the white substance of the brain, but the basal ganglia, cerebellum and spinal cord were spared. In the affected areas there was a noteworthy paucity of microglial macrophages, but an abundance of abnormal neuroglial cells and fibres. Large swollen mononuclear cells—"globoid cells" or "violet cells" (so-called from their colouration with haematoxylin)—were found in both myelinated and demyelinated regions. The suggestion was again made that the primary anomaly in this disease concerns the neuroglial apparatus. The relationship between demyelinating disease of the Schilder type and the lipoidoses received a new bond of connection with the report by Norman (1947*b*) of an example of diffuse progressive leucoencephalopathy, in which abundant metachromatically staining material was found not only in the macrophage cells of the affected white substance, but also in certain symmetrically placed nerve-cell groups (dentate, subthalamic nuclei and certain mid-brain cranial nerve nuclei). These nerve cells were grossly distended with the abnormal substance, and were reminiscent of the cells of amaurotic family idiocy. Moreover, deposits of metachromatic substance were found in the kidneys, which showed chronic nephritis, and also in a papilloma present in an abnormally small gall-bladder. A sister of this patient also suffered from Schilder's disease, and had a similar malformation of the gall bladder. This is the second case of leucoencephalopathy to be recorded in which the deposition of metachromatic material has involved white

matter, nerve cells and viscera. Norman suggests that the metachromatic substance is to be regarded, not as an abnormal breakdown product of myelin, but as the product of a defective synthesis of myelin by the glial cells, in particular by the oligodendroglia. A very unusual type of white matter affection without neuroglial sclerosis was reported in two siblings by Josephy and Lichtenstein (1943). Clinically the disease was characterized by a very slow and prolonged course, spasticity being eventually succeeded by a phase of athetosis, torsion spasm and other extra-pyramidal features. Degeneration was restricted to the white matter of the brain, which was of a semi-liquid consistency, and which exhibited no reactive phenomena in glia or mesodermal tissues. Acute diffuse demyelinating encephalopathy affected two infants described by Friedman (1944). In his first case a jelly-like softening with cyst formation was present in the white matter, the cortex being intact save in its deeper layers. In the second infant, however, the cortex was widely affected, and this case probably belongs to the class of "diffuse degeneration of the grey matter" (of Alpers) rather than to the group of primary diseases of the myelin sheath.

INFANTILE HEMIPLEGIA.

Stewart's (1948) Morison Lecture was devoted to this theme, and gives a comprehensive account of the clinical and pathological features of the hemiplegias of early life. An unusual finding which was present in three of his cases was simple hypoplasia of one hemisphere—an anomaly apparently unassociated with atrophic changes or other histological abnormality. No new light has been shed on the causation of the mysterious and common type of hemiplegia that follows the sudden onset of convulsions in a hitherto healthy child. The lesions in such cases would appear to be the consequence of arterial occlusion, but in the majority of instances the nature of the occlusion remains obscure. Wyllie (1948) has also reviewed the same subject in his presidential address to the paediatric section of the Royal Society of Medicine. He gives a useful summary of the various theories of pathogenesis and, on the whole, tends to favour the hypothesis that some of the acute cases may follow a specific antibody-antigen reaction in the brain. It is well known that patients with infantile hemiplegia who survive for a number of years show a marked stunting of growth in the whole of the paretic side of the body. The work of Penfield and Robertson (1943) has now indicated that this growth asymmetry is associated with lesions of the postcentral cortex. Light has also been thrown by Verhaart (1947) upon a little-known phenomenon found in certain cases of infantile or congenital hemiplegia, namely, the hypertrophy of the sound pyramidal tract. In two such cases this investigator has counted the myelinated fibres of the hypertrophied pyramid. He found that while the total number of fibres in the tract was not increased as compared with normals, there was, nevertheless, an increase in the number of myelinated fibres of large diameter as against the number of fibres of small diameter, which normally form 90 per cent. of the total.

Cerebral hemiatrophy of the Schob type is the subject of a paper by Josephy (1945*b*). Two explanations have in the past been put forward to explain the extensive loss of nerve cells in the third layer of the cortex of such cases. The

first explanation is that of Bielschowsky, who regarded these laminar lesions as the consequence of vascular disturbances occurring during the repeated fits which are a feature of the condition. In some brains an area of more severe destruction or sclerosis has been demonstrated, and it has been suggested that this area has acted as the epileptogenic focus. The second explanation, favoured by Josephy, is that the operative process is degenerative, and that the epileptic fits are conditioned by progressive degeneration of the brain and not vice versa. Moore (1943) has also given a description of a case of hemiatrophy having a somewhat similar history of paralysis following convulsions, which in this instance began at the unusually late age of thirteen years.

INFECTIVE AND TOXIC PROCESSES.

Neal's (1942) book on *Encephalitis*, though primarily of clinical interest, contains a chapter by Stevenson dealing with pathology, in which reference is made to the little understood encephalopathies of neonatal life. Eicke's (1943) article on foetal encephalitis and its relation to the pathogenesis of mental defect is also of considerable interest. Waggoner, Lowenberg and Howell (1943) have stressed the factor of infection that may be of causal significance in certain neonatal encephalopathies that are ushered in by convulsions. They described examples of gross cerebral sclerosis or cyst formation which were apparently unconnected with birth trauma. The important question as to whether pneumonia in the form of a non-suppurative pneumonic encephalitis may cause cerebral damage of a serious character has been considered by Baker and Noran (1945, 1946, 1947). These authors were struck by the great frequency of thrombosis and perivascular haemorrhage in the blood vessels of all their cases. This finding was irrespective of the type of pneumonia present, and suggested that some substance derived from the parenchyma of the lung might possibly accelerate intravascular clotting. Experiments later showed that homologous lung extract injected into animals led to similar diffuse cerebral thrombosis. Toxoplasmic encephalomyelitis has been described by Cowen, Wolf and Paige (1942) in an article of outstanding importance. The condition appears to be widespread in the United States, and its characteristic late sequelae of mental defect, intracranial calcification and focal choroidoretinitis (possibly associated with microphthalmia) should be searched for in this country. Congenital, infantile and juvenile varieties are described. The lesions are widespread throughout the nervous system, and in recent cases the typical miliary granulomas are present. Hydrocephalus may result either from stenosis of the aqueduct or from periventricular necrosis of the central white matter, which leads to secondary enlargement of the ventricles. In infantile cases large subcortical cavities may be found, as in the example of prenatal infection in identical twins reported by Zuelzer (1944). Gross multiple cavitation of the brain, the cortex being reduced in places to a thin membrane, may also be met with in long-standing cases of western equine encephalitis (Noran and Baker, 1943, 1944, 1945). It is probable that a primary arteritis is responsible for this extensive softening of the brain. Similar areas of cystic softening without, however, implication of the blood vessels were also found in one of Rosanoff's (1947) cases of atypical chronic encephalitis.

Cerebral sequelae of acute *rheumatism* have been reported by Bruetsch (1947). Focal proliferation of the intima of the blood vessels leads to occlusion and brain softening, and subsequent mental deficiency or psychosis may arise. Benda (1947*b*) has also described cases in which severe brain damage was associated with chronic rheumatic encephalitis. Neubuerger (1947), however, in an investigation of the brains of ten rheumatic patients, found only mild, sparsely scattered, vascular lesions which were without serious consequences to the parenchyma. These changes, though not so characteristic as those described in heart or lung, nevertheless do reveal an involvement of the connective-tissue elements of the brain in cases of acute rheumatism.

Vascular damage giving rise to extensive encephalomalacia in a five-year-old child was a feature of a case of periarteritis nodosa described by Malamud (1945), who discusses the role of allergy in this condition. Allergic brain changes were also reported by Ferraro (1944) in the following case of severe post-scarlatinal encephalitis. An eleven-year-old boy started having convulsions two weeks after an attack of scarlet fever, and mental defect and generalized spasticity developed. At autopsy the brain exhibited oedema, haemorrhages, thrombosis and softening, the blood vessels showing perivascular infiltrations of lymphocytes and phagocytic cells. Winkelman (1942) has also described another post-scarlatinal case of unusual severity, in which extensive demyelination of the spinal cord was noted in addition to widespread inflammatory reactions in the brain.

The vascular changes accompanying meningeal infections of various sorts and their significance in the pathogenesis of cerebral damage in early childhood is the subject of a paper by Eicke (1947), who has described in detail the inflammatory changes in the walls of veins and arteries which may lead to occlusion of the vessel. According to this investigator 38 out of 50 cases of infantile cerebral palsy showed vascular changes attributable to infections.

Serious mental deterioration following burns is a well-recognized clinical entity (Bender, 1943), and Walker and Shenkin (1945) have studied the cerebral pathology in six patients who, prior to death, all showed disorientation, mania or stupor. A peculiar feature of these cases was that death took place as the result of respiratory failure some time after the patient has apparently safely emerged from the stage of toxæmia. No evidence was found of thrombosis or embolism, and the authors conclude that the fatal brain damage and oedema are the consequence of the action of circulating toxins.

MISCELLANEOUS.

Massive deposition of calcium salts in circumscribed areas of the cerebral cortex was the main pathological finding in the brains of three epileptics examined by Alexander and Woodhall (1943). The benzidine stain demonstrated that the capillary bed in the calcified areas had not been entirely destroyed, and a few undamaged nerve cells had also survived. The authors suggest that such areas act as epileptogenic foci, and that the initial brain lesion was probably caused by a "shower of capillary emboli," the later calcification being due to the combination of blood-borne calcium with phosphoric

acid derived from the lipid breakdown products of tissue destruction. Progressive extrapyramidal syndromes may also follow the more frequently encountered calcification of the corpora striata and dentate nuclei, as in two cases reported by Rand, Olsen and Courville (1943). The process starts in the smaller blood vessels, which become progressively obliterated, leaving behind calcareous granules. In a minority of cases confluent masses large enough to be visualized by X-rays are formed. The authors mention asphyxia neonatorum as a possible causative factor. An authoritative review of the pathological aspects of extrapyramidal disorders has been given by Van Bogaert (1947b), who enumerates the following recognized types: The sequelae of kernicterus, hepato-lenticular degeneration, Hallervorden-Spatz disease, chronic chorea, torsion spasm, torticollis, progressive pallidal atrophy and status dysmelinatus. Reference must also be made to Van Bogaert's (1946) masterly account of the clinical and pathological features of the pallidal and pallido-Luysial atrophies. Van Bogaert (1947c) has also recorded a familial disease characterized clinically by a slowly progressive myoclonic cerebellar syndrome that yielded later to a state of rigidity. Pathological examination of one affected member revealed a combination of cerebello-dentate atrophy, the pigmentary pallido-reticular condition of Hallervorden and Spatz, cortical gliosis, and minor changes of von Recklinghausen's disease. Much the same type of case has also been recorded by Yakovlev (1942) under the heading of myoclonus epilepsy. Roizin and Ferraro (1943) have reported a case of myoclonus epilepsy in which large areas of telangiectasis were situated in the frontal lobes. This article gives much information with regard to the staining properties of the inclusion bodies often seen in the nerve cells in this condition. Two interesting cases of Wilson's disease have been described by Glazebrook (1945). In the first there was strong clinical evidence that the patient's father and probably the father's two brothers had also suffered from hepato-lenticular degeneration. The second case showed a marked increase in the blood copper level, and Glazebrook suggests that inability to excrete Cu may be the specific liver dysfunction that is responsible for the degeneration of the corpora striata. The pathological findings in a case of Wilson's disease have also been described by Bridgeman and Smyth (1944). A report on the value of liver efficiency tests in the diagnosis of Wilson's disease is a feature of the article by Homburger and Kozol (1946), who found the cephalin flocculation test to be the most sensitive indicator of liver damage.

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SCHIZOPHRENIA.

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INTRODUCTION AND THEORY.

It has to be said that if we ignore the fields of genetics and cerebral surgery, there have been no major advances in the study of schizophrenia during the last five years. Two schools of psychiatry follow their separate paths. In Europe, the teachings of Kraepelin and Bleuler continue to be remembered and research is mainly based on the belief that schizophrenia is a genetically-determined disease entity having an organic basis. Kretschmer (1948) is the senior author of a valuable survey of German psychiatric publications for the years 1939 to 1946. A chapter on schizophrenia is included. The present review quotes papers from this survey and includes some work published earlier than 1944, because the sources have only recently become available to British readers. In America, the hitherto paramount influence of Meyer's school of Psychobiology is being weakened by the new Dynamic Psychiatry which has a strong psychoanalytic bias. This school neglects diagnosis, depreciates heredity and lauds interpretation. It regards schizophrenia as the end-result of maladaptation to psychic traumata (Massermann, 1946).

The dynamic approach has inspired other fictional studies and the passing fashion of cinema and novel to depict psychiatric subjects has not ignored schizophrenia. Indeed, Mr. Ivor Brown (1949) has recently felt obliged to protest against the misuse of the word "schizophrenic," which is now part of the stock-in-trade of critics of the arts. The reasons for the fashion are readily determined. The present time is an age of anxiety, and for all anxieties psychoanalysis offers an explanation, with sometimes an outlet and less often a cure. Now no one, not even a trainee analysand, reveals his complexes so shamelessly as does the schizophrenic. It is understandable, therefore, that the public will avidly devour fictional and biographical descriptions of schizophrenia, especially if the fictional psychiatrist and patient are fitted into the eternal triangle. The best real-life descriptions of schizophrenics, such as Freud's study of Dr. Schreber (1925), and the self-description of Professor Ludwig Staudenmaier (1912), were caviare to the general, for they came before the popular taste had been whetted.

Mine Own Executioner, by N. Balchin (1946), is an expertly written tale of a lay psychotherapist's efforts to stay the development of a schizophrenic psychosis. The novel and its film version put forward an apologia for lay therapy which is turned into an indictment by the inexorable progress of the

psychosis. In *The Snake Pit*, Mary Jane Ward (1947), has given a partly autobiographical account, recollected in tranquillity, of a schizophrenic illness, but the main interest of this best-seller and of its sensational film version lies in its description of conditions in American State hospitals. Under an equally repellent title, J. F. Bardin (1948) has written a psychological novel which vividly and sensitively describes the subjective life of a schizophrenic. The heroine's ambivalence, primary delusions, ideas of reference, passivity feelings and emotional accesses are sympathetically drawn with unusual insight and accomplished literary craftsmanship. If the picture fails to be convincing it is because the schizophrenic's inner life almost defies description. The disease has such dire effects on volition and thinking that the writings of schizophrenics rarely reach print, and such as do are almost always the products of paranoid schizophrenics. One who showed rare productivity was August Strindberg, the centenary of whose birth fell in 1949. His largely autobiographical writings are rich in clinical material, and the recent biography by Miss Elizabeth Sprigge (1949) should be read by every psychiatrist. J. A. H. Ogdon (1947) has described the circumstances of his certification and detention, and his self-cure by the practice of Yoga. Such writings usefully remind us that the patient is an individual who can respond to sympathy and understanding, even when his personality is disturbed by the schizophrenic illness. However, this can equally well be said of any illness, physical or mental, and does not imply that psychogenic and environmental factors are the cause of schizophrenia.

Gjessing (1946), in an introductory lecture to the 8th Congress of Scandinavian Psychiatrists, has given his views on the methods of biological research in schizophrenia. The *aim* of such investigations in a large field, such as schizophrenia, is usually to form a hypothesis regarding the development of the essential features and then to try to verify the hypothesis by random tests in an appropriate field. In dealing with a disease of unknown pathogenesis, Gjessing believes that the adoption of a hypothesis, followed by examination of a large group of patients, is not a suitable approach, because it is not known if the patients belong to the same pathogenetic class. If, however, a small exactly defined field of enquiry is selected and examined thoroughly, valid conclusions may be reached. In this approach one dispenses with a preliminary hypothesis and confines oneself to a description of what is actually taking place.

The *plan of work* consists in surveying, without any preconceived notions, the disturbances of bodily functions that have been noted in the individual patient. It is important first to rid the patient of any complicating exogenous factors, such as infection, and to continue to see the patient daily, as well as to see the results of daily investigations. A start is made with one patient and later others are added who show the same functional anomalies of body and mind. Finally, a primary homogeneous case-material is available. Thus, the criterion of selection is not a psychiatric label, but a definite psychic and somatic functional disorder. Subsequently, questions may be asked and tests of function undertaken because the patient's own functional range during the spontaneous course of the disease can be employed as control. The *means*

must always be adjusted to meet the particular problem presented in the situation as it exists. An attempt must be made to grasp and characterize the functional changes in the field that is best adapted for qualitative characterization and quantitative evaluation. The field may be physical, chemical, serological or enzymological.

It is Gjessing's opinion that serial study of body functions in a few patients who serve as their own controls is a more valuable mode of investigation than the more usual hypothesis-verification approach. Hemphill and Reiss (1948) have also stressed the difficulties of research that are involved when under the label of schizophrenia are grouped cases of unknown aetiology that may be similar in prognosis and psychopathology but otherwise dissimilar. Their biochemical investigations on schizophrenics show many cases producing constant results and many producing inconstant results; this means that variation in test results must be expected unless the patients are in the same stage of the disease or are suffering from the same type, but these conditions are clinically not yet ascertainable. Their work, and that of Gjessing, has certainly been more productive than the labours of Hoskins (1946) and his associates at the Worcester State Hospital. In the Salmon lectures for 1945, published under the title "The Biology of Schizophrenia," Hoskins began his review with a consideration of the atom and proceeded to depressingly meagre returns for 18 years of exhaustive investigations into the physiology of schizophrenics. Although numerous minor physiological differences of a quantitative kind have been found, Hoskins' summing up is the generalization that schizophrenia is marked by many defects in adaptive efficiency. He believes that a fundamental characteristic of the psychosis is the patient's failure to achieve or retain an adequate breadth and depth of empathy, and in those patients who remit he has been impressed most by the improvement in empathy. This is common experience and underlines the need to foster the patient's contact with the social environment after remission.

Meduna and McCulloch (1945) have aimed to separate recoverable, schizophreniform, symptomatic, reactive, or pseudoschizophrenic states from true endogenous schizophrenia. They believe that patients in the former group have a disorder of the sensorium, because after remission they describe their illness as "like a dream," or as "like a scene from the theatre in which everyone was playing a part." Bleuler's third criterion of schizophrenia, absence of disorder of the sensorium, would exclude the above remitting cases, so Meduna and McCulloch propose to give the name Oneirophrenia to those psychoses which fulfil Bleuler's criteria of associative and affective impairment, but which do have some clouding of consciousness. The onset is acute, and the clinical picture shows some clouding of the sensorium ranging from mild disorders of perception and recollection to hallucinosis. Biochemically, the psychosis is characterized by (1) resistance to insulin; (2) a pseudo-diabetic reaction to the Exton-Rose test and a protracted sugar tolerance curve during the intravenous glucose tolerance test; and (3) the presence of an excess of anti-insulin factor in the urine (Meduna and Vaichulis, 1948). In oneirophrenia the prognosis is usually good for spontaneous remission and in response to convulsant therapy.

Gaupp (1942) is one of the few senior Continental psychiatrists who still believe that Paranoia exists as a separate diagnostic entity in the Kraepelinian sense. In the 1944 edition of their textbook of psychiatry, Henderson and Gillespie have decided to group the paranoid type of schizophrenia along with paranoia and paranoid reaction types, on the grounds that the pre-psychotic personality is not necessarily schizoid and that the paranoid types do not terminate in schizophrenic dementia. Some support for separating the paranoid group is afforded by the studies of Hemphill *et al.* (1944, 1945 and 1948), who found no testicular atrophy in their paranoid schizophrenics, and by Hauptmann and Myerson (1948) who found normal capillary structure in their paranoid cases.

In a thoughtful paper, Stengel (1945) has studied the clinical relationship between obsessional symptoms and schizophrenia. He points out that when schizophrenia develops in one who is an obsessional neurotic, the resulting picture tends to be simple or paranoid; the integrating influence of the obsessional personality seems to prevent the appearance of catatonic or hebephrenic reactions which necessarily involve personality disintegration. In Stengel's case-material the psychosis often resulted in release of primitive impulses which had previously been kept under control with the help of obsessional symptoms; regressive conduct, such as coprophagia and exhibitionism, did not therefore carry the malignant prognosis one would expect. Again, because of the obsessional's habitual preoccupation with the testing of reality he does not give himself up unquestioningly to his delusions and hallucinations. Malignant progressive deterioration appears to be unusual when schizophrenia develops in an obsessional personality: the structure of the obsessional personality counteracts the schizophrenic process. The life of August Strindberg exemplifies these principles.

A side-effect of the modern physical treatments is likely to be the return to society of a larger number of schizophrenics who show arrest of the disease along with some defect of personality. Until a hundred years ago such eccentrics added to the interest of life, but modern society and the modern family are less tolerant of mental aberration, while forensic responsibility is of greater moment. Feldman *et al.* (1947) point out that greater socio-economic problems have emerged along with the partial successes of the physical therapies, and that there has been a subtle shift of responsibility for the care of the patient from the state to the family, which may also require to make material changes in living conditions. Zuring (1946) has studied this problem in the families of 304 married schizophrenics who were discharged from hospital between the years 1933 and 1942. Only a few patients married after discharge, and only 16.7 per cent. of 670 children were born after the first attack of schizophrenia. The majority of patients reacted favourably to their home surroundings without causing any disturbance of family life. It was among the upper social classes that the patient's behaviour tended to cause family strife and interference with the education of children. With efficient after-care such problems should not bulk large.

Bellak (1948), in a volume devoted to *Dementia Praecox*, has summarized and briefly evaluated some 3,200 papers published during the period 1936 to

1946. Gillies (1949) has contributed a chapter on the schizophrenic disorders to a volume intended for general practitioners and medical students.

AETIOLOGY.

Hereditary factors are discussed in another chapter of this survey.

In view of doubts regarding the biological unity of schizophrenia, M. Bleuler (1948a) has studied the basic personality on which the psychosis was grafted. His case-material consisted of several large families, and he found that if schizophrenia developed from a schizoid personality in one family, then the same type of personality was present in other members of the family who later became psychotic. The same held true where the psychosis developed from an obsessional, hysterical or other psychopathic personality.

He has also made an investigation of small subgroups of schizophrenics who showed stigmata of endocrine dysplasia, and he included a study of the blood relatives of his patients. In a number of schizophrenics he found what he calls acromegaloïd signs, such as high stature, heavy physique, and large nose, chin, ears, tongue, hands, feet and genitalia. These physical features proved, to some extent, to be genetically linked with the psychosis in the families that were investigated. The incidence of schizophrenia in the acromegaloïd subjects was three times greater than the incidence in the other members of the family. In the non-psychotic acromegaloïd subjects Bleuler also found a characteristic personality deviation which he attributed to a disturbance of balance in diencephalic-pituitary function. He admits, however, that as this endocrine dysplasia is found in less than one per cent. of schizophrenics it cannot have great significance for the aetiology of schizophrenia.

Some of Bleuler's co-workers (1948b) have conducted research on the same lines, and have studied the combination of schizophrenia with Cushing's syndrome and other endocrine abnormalities. From these extensive and intensive investigations some interesting details emerge, such as the influence that endocrine obesity, virilization and their associated mental characteristics exert on schizophrenic symptomatology, but no important discoveries have been revealed on the aetiological or pathological problems of schizophrenia.

Rosenzweig and Bray (1943) studied the life-histories of 124 schizophrenics, 102 manic-depressives, 130 dementia paralytica patients and 250 normal subjects, all of the male sex, and found that the number of the patient's siblings who died between the patient's birth and nineteenth birthday was significantly greater in the schizophrenic group than in any of the other groups. However, in a later study on females, Blum and Rosenzweig (1944) found negligible differences.

Malamud and Malamud (1943) have made a socio-psychiatric study of schizophrenia in the American armed forces and find that the screening process at enlistment could have eliminated more than half of these cases if a minimum amount of easily procurable data of their history had been available. As to the part played by service stress in causing the schizophrenic illness, they find that the material can be arbitrarily divided into certain groups. In some of them constitutional or perhaps metabolic factors may be the determinants, and the military situation is, at most, only of precipitating importance, so that,

in this respect, they can be aligned with the psychopathic personalities. In others of the schizophrenics the factors in the military situation show a closer relationship to the social and psychological experiences in the life of the person. The latter group, along with the psychoneuroses, appear to be dynamically strongly dependent upon the stress produced in the Army. The authors' approach is, of course, in the Meyerian tradition and heavily underlines the obvious.

Because of the alleged affinity between tuberculosis and schizophrenia, and the possibility that the relationship is causal, Alstrom *et al.* (1943) have made a painstaking study in 525 males and 501 females. Active tuberculosis was present in 8 per cent. of male, in 5.2 per cent. of female schizophrenics, and in only 2.7 per cent. of a heterogeneous group of non-schizophrenic psychotics. The catatonic patients had the highest incidence of active tuberculosis. The incidence of uncleanness, refusal to take nourishment, and dementia was also higher among the patients suffering from catatonia than in the other groups. There was, however, no difference in the frequency of active tuberculosis between the catatonics displaying these symptoms and those who were free from them. Infection within the institution cannot reasonably be the cause of the higher frequency of tuberculosis in the catatonic patients. The schizophrenic patients showing signs of hebephrenia or paraphrenia to begin with, and later passing over to the catatonic form, showed the same frequency of tuberculosis as those affected with catatonia from the beginning. There is a relationship between loss of weight and the development of tuberculosis. The weight loss is due, not to the tuberculous infection, but to the catatonic illness, and when weight increased the tuberculous infection tended to improve.

Hauptmann and Myerson (1948) studied the capillaries of the fingernail fold in 75 schizophrenics and 37 manic-depressives and found striking differences. In 71 per cent. of the schizophrenics the capillary formation was immature and similar to that seen in normal infants. In 78 per cent. of the manic-depressives the capillaries showed tortuosity, which is also a feature of constitutional neurotics. None of 10 undeteriorated paranoid schizophrenics showed the immature formation; instead, either normal or tortuous capillaries were seen. In one case the normal sibling of a typical schizophrenic showed the characteristic picture of immaturity. The authors link up their findings with Hoskins' view that immaturity is one of the most outstanding features of schizophrenia. Unlike Olkon (1939), who studied the triangular space between thumb and forefinger, the authors did not find that the capillary picture altered with changes in the clinical picture of the psychosis.

PATHOLOGY.

(a) *Metabolic and Biochemical Factors.*

Although the majority of studies have been fact-finding and concerned with isolated observations that have no clear relationship to the problem of schizophrenia, Scandinavian workers have tried to relate their experiments to the actual disease.

Gjessing (1947) has met criticisms of his well-known work on periodic catatonia by further experiments. Thus the negative nitrogen balance in

his patients might be due to motor excitement. That this is not the case is shown by measuring the motor activity with the aid of a seismograph, which demonstrates that the excess nitrogen excretion begins days or weeks before motor excitement starts.

Further, the phasic variation in N-excretion raises the question whether there is impairment of kidney function, such as has, according to Gjessing, been found in melancholia. Kidney function tests suggest there is no organic renal lesion.

Another field of enquiry is offered by the dramatic alterations in the physical condition accompanying the change from stupor to excitement. A predominantly cholinergic vegetative state alters to an adrenergic state with anisocoria, mydriasis, salivation, pallor, tachycardia, inhibition of peristalsis, sphincter spasm, paralysis of the detrusor of the urinary bladder, sleep disorders, etc. The question thus arises, is this spontaneous alteration in vegetative function due to an endogenous noxa which reaches the central nervous system through the blood stream, and perhaps has its origin at the periphery, and acts partly at the periphery and partly on central organs?

Kjaestad (1942) conducted E.C.G. examinations in a case of periodic catatonic stupor, on which patho-physiological studies had been made and published by Gjessing. Electrocardiograms were taken during five periods of stupor and during the intervals. The amplitude of the waves was measured. In all five periods T₁, and in four periods of stupor, T₂, were found to be isoelectric, and in the fifth stupor to be very low. These findings are not present throughout the whole period, but in the majority of cases occur at the beginning of a stupor when it is at its deepest. There was a marked parallel synchronicity between the height of the T wave, the psychological condition of the patient, the oxygen consumption, and a number of other changes found by Gjessing. When the oxygen consumption was large the isoelectric T. wave was most frequent. The E.C.G. was often found to be similar to that occurring in myxoedema. At the beginning of the stupor the periodic nitrogen retention reached its highest value and afterwards nitrogen was excreted.

From these studies and from experiments with amyl nitrite, thyroxin, changes in posture, and the comparative studies of metabolic changes of the patient, and since none of the usual causes producing an isoelectric T wave was found, Kjaestad is inclined to conclude that these reversible abnormalities of the E.C.G., synchronous with the deepest stupor, are not produced by cerebral means, but are directly due to the metabolic disturbance (a change in the cellular metabolism of the myocardium or the action of humoral noxae on the myocardium). These findings confirm that the psychosis is not only a disease of the cerebrum, but a general disorder.

On the other hand, the muscular rigidity which occurs especially in the first half of the stuporous phase is probably centrally determined. Gjessing quotes H. Seyffarth, who has conducted clinical and electromyographic investigations and finds that the rigidity is apparently free from oscillations, that is, is not due to tetanic contraction. Nor is it associated with a particular state of consciousness or hallucinosis. It seems to be of the same nature as the rigidity of extrapyramidal lesions, though it is, of course, reversible.

Caloric nystagmus has been investigated by Lowenbach, also quoted by Gjessing. In the stuporous phase an extremely low number of twitches occurs, and sometimes there is only a single slow deviation movement such as is seen in some narcotic and toxic states. The frequency is always, even in lucid phases, less than 1 per second, whereas normal controls show more than 1 per second. The number and duration of the twitches for cases of catatonic excitement were concordant with the findings in catatonic stupor.

Gjessing reports finally on a simple psychic function, the rapidity of reaction to standard acoustic and optic stimuli. The results show an increase of the average reaction time in the phase of catatonic excitement though this increase is not seen in every reaction. Rapid reactions sometimes do occur and suggest that it is the power of concentration that fails.

In their cytochemical investigations Hyden and Hartelius (1948) have found that, in connection with sensory and motor stimulation, the nucleoproteins of the nerve cells undergo extensive katabolism followed by restitution. This metabolism is governed by a special protein-forming system in the nerve cells. The nucleoprotein metabolism in the nerve cells is thus associated with the motor and sensory functions of the neurons (Hyden, 1943). It is probable, but so far not established, that the same correlation exists for the psychic functions. To influence the nucleoprotein content of the ganglion cells of the central nervous system use was made of malononitrile, $\text{CH}_2(\text{CN})_2$. Quantitative studies were made, by microspectrographic methods, of the nucleoprotein content of the nerve cells of rabbits. Small doses of malononitrile were shown to increase the amount of nucleic acid of the ribose type in the nerve cells from, on an average, 1.7 per cent. to 3.1 per cent. The ratio of nucleic acids to protein substances changed from 1:7 to 1:35. This was demonstrated in the pyramidal cells of the cortex and in other cells of the central nervous system. Malononitrile stimulated the nerve cells to an increased production of nucleoproteins. Pyramidal cells with a poorly developed nucleolar apparatus and a low content of nucleic acids and protein substances (as a sign of decreased nucleoprotein metabolism) were found in large numbers in the frontal cortex (Lamina III) of persons suffering from psychoses. The material for examination was taken during frontal lobotomy, performed on 10 cases of schizophrenia and 1 case of endogenous depression. It was assumed that the lowered nucleoprotein metabolism was an effect of the psychosis, but it has to be remembered that previous shock treatments may have produced changes in cellular structure and function, and in any case, Meyer and Meyer (1949) have recently shown that the abnormal cells found by Hyden and Hartelius are well-recognized artefacts of biopsy technique. However, the results obtained in animals led the authors to consider whether malononitrile could stimulate function in such nerve cells in addition to increasing nucleoprotein. (See under "Treatment.")

By means of a metabolic hypothesis, Meduna *et al.* (1943) have made yet another attempt to break down the boundary line between affective and schizophrenic disorders. They refer to the widespread belief that one of the underlying factors in schizophrenia is a disordered metabolism, which does not, however, determine the form taken by the psychosis. The actual clinical picture is held to be shaped by the pre-psychotic personality. They point to

the patients who, first regarded as manic-depressive cases, later turn out to be schizophrenics. In schizophrenic, and also in other functional psychoses, the authors have found that the administration of d-laevulose produces blood-sugar curves of three different types. From this slender evidence they suggest that the same pathological disorder of carbohydrate metabolism underlies both schizophrenia and manic-depressive psychosis, and they point out that patients of pyknic habitus and extraverted personality who develop schizophrenia almost all recover spontaneously or after treatment.

A more cautious approach to carbohydrate metabolism in schizophrenia is made by Katzenelbogen *et al.* (1944), who have estimated the glucose, oxygen and carbon dioxide contents of arterial and venous blood in 12 undoubted schizophrenics. The number of cases studied was small and the glucose levels were estimated by the somewhat inaccurate technique of Folin. Wisely, and indeed inevitably, the authors hesitate to interpret the following contradictory results. They found a relatively low sugar content of both arterial and venous blood which suggests that there is a lower intracranial carbohydrate metabolism. However, their findings of higher differences in the sugar contents of arterial and venous blood than in normal subjects suggests a more intense carbohydrate metabolism in schizophrenics. A lower average venous-arterial difference in carbon dioxide content in the schizophrenics than in normal subjects suggests that the cases under examination had a lower carbohydrate metabolism. Some of the patients showed a lower intracranial oxygen metabolism.

Kety *et al.* (1948) have measured the cerebral blood flow in 22 schizophrenic patients by the new nitrous oxide technique and have found it to be within the normal limits, as was the oxygen consumption. Intravenous sodium amytal producing clinical improvement was not accompanied by any measurable change in cerebral blood flow or oxygen consumption. During insulin coma there was a progressive decrease in cerebral utilization of oxygen and blood glucose, while the cerebral circulation remained unimpaired. E.C.T. is followed by a moderate decrease in metabolism and a marked decrease in cerebral blood flow along with a severe acidosis, probably due to the anoxia and muscular exercise.

Hoskins (1946) asserts that the only correlation that has appeared with any consistency in blood-sugar studies is that between degrees of emotional tension and the abnormal glucose reactions.

Kasin and Parker (1943) have given a detailed account of a male schizophrenic who developed true diabetes mellitus 9 years after the onset of his psychosis. The patient's race is not stated, and, needless to say, he was not given insulin coma treatment, but a brief increase in lucidity and contact with the environment followed an accidental hypoglycaemic episode. Although the association of diabetes and schizophrenia is rare, Ligterink and Simons (1936) found 6 cases among 279 Jewish schizophrenics, and they pointed out that their cases had the pyknic habitus and a hereditary taint of manic-depressive psychosis.

De Jong has devoted the last 25 years to the study of experimental catatonia and has now incorporated his findings in a book (1945). He describes the production of catatonia in animals by bulbocapnine, mescaline, adrenaline,

acetylcholine, asphyxiants of the central nervous system, and other chemical and physical agents. Catatonia is regarded as a general mode of reaction of the central nervous system and hence is of varied aetiology although schizophrenic catatonia is the commonest example. De Jong considers that his experimentally-produced catatonia in animals is comparable to human catatonia and that there is a striking similarity between the hypokinetic, hyperkinetic, and autonomic signs of the two conditions. The only metabolic changes producing catatonia in animals were those accompanying dysfunction of the liver and intestines, and the old view that auto-intoxication from the bowel was the cause of schizophrenia is resurrected.

It will be remembered that Quastel and Wales (1940) found an agreement between catatonia and pathological reduction of hippuric acid excretion. Their findings are still debatable. Michael *et al.* (1944) studied the rate of synthesis of hippuric acid and of concomitant changes in the excretion of uric acid, and in the levels of pyruvic and lactic acids in the blood in 18 schizophrenic patients and in 9 normal control subjects. The average amount of hippuric acid synthesized in four hours was approximately the same in the two groups. Three schizophrenic patients synthesized amounts considerably less than the lowest value for the normal subjects, while 3 patients exceeded the range of the normal subjects. Unlike the normal group, several of the schizophrenic patients showed initial retardation in the rate of synthesis, and 2 patients excreted unusually large amounts of hippuric acid during the first hour of synthesis. The ingestion of sodium benzoate caused a retention of uric acid which was slightly higher in the patient group. The synthesis of hippuric acid was accompanied by changes in the level of pyruvic acid of the blood. It is pointed out that the rate of synthesis of hippuric acid is believed to be correlated with body size. If corrections had not been made in the author's figures there would have been a considerable difference in favour of the control group in the average amounts synthesized during the test period. No interpretation could be offered for the difference in retention of uric acid nor for the shift in the pyruvic acid level. The results indicated that most schizophrenics, catatonics included, have adequate ability to detoxify benzoic acid. On the other hand, Koersner (1946) studied 69 cases of schizophrenia and 28 normal persons and found a reduction in hippuric acid in many catatonic cases especially where the psychotic phase was active. He concludes that in certain catatonics a reduced power of detoxicating benzoic acid is present, but points out that it is doubtful whether his results are expressive of a liver injury connected with the schizophrenic disease: the results might mean an altered protein metabolism due to new needs which must be met by the liver while the schizophrenic psychosis is developing.

Katzenelbogen and Snyder (1943) have analysed the blood cells and serum of schizophrenic patients for sodium, potassium, calcium, magnesium, inorganic phosphorus and chloride. As compared with results they previously obtained from 12 normal subjects, the present study showed slight elevation of serum potassium in schizophrenic patients and of the chloride and inorganic phosphorus contents of the cells in one case each. The other mineral values were within the ranges of their normal group. The difference between some

of their values and those of other investigators may possibly be attributed to the differences in the emotional state of the patients at the time the specimens of blood were obtained.

Using an improved method of analysis, Wikoff *et al.* (1945) seek to prove that there is a significantly lower concentration of bromine in the blood of schizophrenic patients than in normal controls. Although comparative tables are not included, it does not seem likely that the admitted standard deviation of .2 mgm. per cent. (between the means of .555 and .81 mgm. per cent.) would support the contention.

The time-worn search for a toxic factor in schizophrenic serum has been resumed by Sjovald (1946). He found that haemoglobinaemia in mice followed the injection of serum from both schizophrenic and normal persons, but he was satisfied that the haemolytic effect of schizophrenic serum was significantly greater, and he assumes that schizophrenics have an abnormally large amount of a haemolytic factor which is present in normal persons.

(b) *Endocrinological Factors.*

It has long been suspected that endocrine factors may be closely related to the production of schizophrenia, and Kraepelin himself believed that the gonads were at fault. Recent studies by Hemphill and his colleagues have given new impetus to such research and have led to therapeutic attempts to replace deficiencies in hormone secretion. Other workers have devoted their investigations to disorders of the adrenal cortex and have observed the therapeutic effects of adrenalectomy in cases associated with virilism. Finally, Manfred Bleuler and his school have thrown some light on the connection between endocrine dysplasia and schizophrenia. (See under "Aetiology.")

Hemphill *et al.* (1944, 1945 and 1948) have made histological studies of biopsy specimens of the testis in 90 schizophrenics and 25 cases of other mental disorders. A special form of atrophy of the tubules was found in many cases of schizophrenia. The method of study seems to have avoided the errors that led to the rejection of Mott's well-known contribution to testicular histology in dementia praecox. The severity of the testicular changes was proportionate to the severity of the psychosis except that in paranoid schizophrenia no significant degree of atrophy was found. (Morse's studies, rebutting Mott's findings, were conducted on paranoid cases.) It is not suggested that the testicular lesions are the cause of schizophrenia but that both they and the psychosis are results of the causal process which is perhaps mediated by the hypothalamus or pituitary. This important work recalls that of Stiasny and Generals (1937) who studied the spermatozoa of schizophrenics at the time of sterilization, and found abnormal morphology in 53.8 per cent. of cases compared with 1 per cent. in normal men.

Hemphill and Reiss (1945) have used gonadotrophic hormone from pregnant mares' serum in the treatment of eighteen male schizophrenics who showed histological evidence of atrophy of the testis. Two hebephrenic patients recovered after some 6 weeks' intensive treatment: 1,000 units of gonadotrophin were injected daily. Several of the patients showed considerable

regeneration of the testis with increased cell division and increase in the size of the tubules. The final stages of spermatogenesis were not promoted, and there was no evidence of an increase in mature sperm production. A hebephrenic female recovered after similar dosage. Although the method is expensive the results are sufficiently interesting to warrant further trials in early cases.

In a careful fact-finding study of 453 female schizophrenics and 810 female surgical patients, Lohse and Bjarnhjeldinsson (1945) found an increased frequency of hypertrichosis in schizophrenic women. Hypertrichosis was present in 60 per cent. of the schizophrenics and in 36 per cent. of the controls. Proceeding from this study, and assuming that the output of androgen is related to the occurrence of hypertrichosis in women, Pedersen (1946) investigated androgen metabolism in schizophrenic women who were not hypertrichotic. A colorimetric method was used to estimate androgen excretion in 10 normal-haired schizophrenic women, 33 hypertrichotic schizophrenic women, 2 hypertrichotic women with other psychoses, and 19 normal women with normal hair distribution. The results showed a tendency to increased androgen excretion in the hypertrichotic women, whether schizophrenic, otherwise psychotic, or mentally normal. There was no such tendency in schizophrenic women with normal hair growth. Pedersen concludes that the androgen output *per se* seems unlikely to have any pathogenetic significance in schizophrenia, though, of course, other functions of the adrenal cortex may be involved. Allen and Broster (1945) have reported the case of a woman, aged 26, who had been thoroughly treated over the previous two years with E.C.T. and insulin coma, but had continued to show features of catatonic and paranoid schizophrenia. After her schizophrenia had been present for eighteen months she became hypertrichotic. Removal of one adrenal, which showed a positive ponceau-fuchsin reaction, produced immediate and lasting mental improvement, and the daily urinary steroid excretion fell from 30 to 7.2 mgm. This is a remarkable case though, of course, one cannot be sure that the recovery was not due to a spontaneous remission.

Dax *et al.* (1947) have described a woman with long-standing adrenal pseudo-hermaphroditism who later developed schizophrenia. Removal of one adrenal gland resulted in lowering of the urinary steroids from 20 to 7.4 mgm. per day but did not effect any change in the patient's mental or physical state. The authors point out that the relationship between a specific endocrine abnormality and psychiatric disorder may be in the following ways: (1) The mental illness may be the direct result of the glandular dysfunction; (2) the mental illness may cause the glandular dysfunction; (3) the mental illness and the glandular changes may coexist independently; (4) the mental illness may be psychogenic in response to worry over the physical changes induced by the gland; and (5) the mental illness may be the result of secondarily induced changes in other endocrine glands.

(c) *Morbid Anatomical Factors.*

As is to be expected from previous studies, the findings in this field are largely negative.

Under the misleading title "Fatal cerebrovascular accident associated with

catatonic schizophrenia," Murphy and Neumann (1943) describe the case of a man, previously mentally stable and physically healthy, who became acutely excited and after a week sustained a hemiplegia. After 5 days in stupor he died on the 12th day of his illness, and post-mortem examination showed a thrombosis of the left middle cerebral artery. There is no justification for attaching the name of schizophrenia to such symptomatic psychoses. Ferraro (1943) has published the similar case of a youth who was diagnosed as a hebephrenic schizophrenic, despite absent knee jerks and a unilateral extensor plantar response. Following cardiazol treatment he twice went into status epilepticus. Three years later he died suddenly of pulmonary oedema, and post-mortem examination of the brain showed generalized cortical atrophy and diffuse demyelination. Neither air encephalograms, electroencephalograms nor examination of the cerebrospinal fluid were undertaken in this organic psychosis, and yet the author claims that his case supports the trend to consider schizophrenia not as a disease entity, but as a syndrome which may arise from several aetiological factors. Yet another case of "Schizophrenic reaction syndrome in the course of acute demyelination of the central nervous system" is described by Roizin *et al.* (1945), and the authors are at pains to stress that they do not aim to put forward an organic aetiology for schizophrenia, but merely to illustrate that somatogenic factors may sometimes precipitate an acute psychosis. This fear of flirting with somatogenesis is a feature of so-called dynamic psychiatry.

Kirschbaum and Heilbrunn (1944) have made biopsies of the cortex and adjacent white matter during prefrontal leucotomy operations on physically healthy schizophrenics. In one case negligible changes were found, though the patient had been psychotic for 17 years. In the remaining 10 cases pathological changes such as vacuolation, swelling or shrinking of ganglion cells, hypertrophy and pyknosis of the glia, and fatty deposits in the ganglion cells and vessel walls were evident. These latter changes were not found in the brains of two non-psychotic patients who had died during laparotomies performed under ether anaesthesia, and they were found in one case of the series who was anaesthetized with Pentothal. The authors point out, however, that the brains of young healthy non-psychotic persons may show fatty infiltration and therefore only massive deposits should be considered pathological. The shock therapies tend to cause fibrous proliferation of glia cells, and this constitutes another source of confusion in the histology of the schizophrenic brain. The traumata of biopsy and of subsequent histological technique are also likely to induce artefacts.

Kluge (1943) believes that the liver changes found by Gaupp (1940) during the post-mortem examination of schizophrenics have no significance. Similar changes were found in cases who died of hunger oedema, brain tumours and meningitis, and the findings seem due to inanition and the process of dying.

(d) *Miscellaneous Factors.*

May (1948) has examined 343 male schizophrenics and 100 mentally normal males for pupillary inequality and for pupillary reaction to pain and light. A high incidence of abnormality was found in the schizophrenic group and was

concluded to be closely related to the pupillary changes that occur during muscular effort, and which are thought due to simultaneous sympathetic stimulation and parasympathetic inhibition originating in the hypothalamus. The pupillary reactions seem to be an example of hyporeactivity.

Fleischacker (1943) has investigated the Schrijver-Bernard toe-flexor reflex in 75 normal persons and in 82 mainly catatonic schizophrenics, and has found the reflex present five times more often in the catatonic schizophrenics than in other functional psychoses. The reflex is positive if percussion of the tibia causes plantar flexion of the small toes.

Lehrman and Weiss (1943) report a case in which narcolepsy was associated with paranoid schizophrenia. The association of the two diseases is not common, and all the reported cases have been paranoid schizophrenics. In this case the narcolepsy was present for 13 years before the psychosis began, but the pre-psychotic personality was schizoid. The delusional content of the case was originally concerned with the attacks of sleep, and when the narcolepsy responded to benzedrine the delusions ceased to be concerned with the attacks of sleep, but became more diffuse.

Leys (1946) has reported two cases of acute rheumatism and Sydenham's chorea in which psychotic symptoms were prominent. Although these symptoms were distantly reminiscent of schizophrenia, there is nothing in the scanty case-records to controvert a diagnosis of organic psychosis due to rheumatic encephalopathy. Similar cases have been described by Bruetsch (1940, 1947) and by Van der Horst (1948).

PSYCHOPATHOLOGY.

Studies in this field have utilized both experimental and philosophical approaches.

Thought-disorder, one of the most prominent and diagnostically reliable symptoms of schizophrenia, has recently been termed disorder of conceptual thinking. It was first experimentally investigated by the Russian psychologist, Vigotsky, who concluded that the essence of the symptom was loss of ability to think in abstract concepts and a regression to "thinking in complexes." Hanfmann and Kasanin (1942) have largely confirmed Vigotsky's conclusions. Similar studies have been reported by Goldstein (1943) who used a battery which included the object-sorting test, a modified Kohs' blocks test, the Vigotsky test and the Rorschach test. The work is an extension of the author's researches on organic brain lesions. The most significant finding was that in certain schizophrenics there is a characteristic impairment of the attitude to the abstract, so that the patients behave much more concretely than normals. Examples are given from schizophrenic symptomatology and language. Goldstein discusses the similarities between thinking in schizophrenia and in organic brain disease, and the question whether the schizophrenic impairment in abstract attitude is a primary or a secondary phenomenon. Finally, he suggests that, on theoretical grounds alone, psychotherapy cannot be effective unless the approach takes account of the patient's preference for the concrete and is adapted to his capacities, or until the attitude has been altered by shock therapy or remission.

Whitehorn and Zipf (1943) have made an original use of a statistical technique of philological research. It is known that in standard usage of language the frequency with which the different words in a sample occur is related mathematically to the ranks of the words when these are arranged in order of decreasing frequency (in English "the" ranks as 1, and "of" ranks as 2). The mathematical relation approximates to an equilateral hyperbola. Using this criterion, by its straight-line expression on logarithmic graphs, the authors have studied the personal letters of a paranoid schizophrenic. Her language-behaviour graph showed a rigidly systematic deviation from the normal curve in the direction of a consistent, straight and uniform steepness which the authors interpreted as an expression of an autistic speech tendency. They point out how autistic people become verbally and conceptually handicapped in solving test problems, and real problems also, because they use language in their own private way and do not trouble to meet the normal demands of social serviceability.

In a monograph, Shakow (1946) has reported the psychological study of 25 schizophrenics by the application of a battery of verbal and apperceptive tests, certain studies of reactions in semi-naturalistic situations, and various studies of motor and learning functions. He finds that there is a widespread disturbance of psychological function which does not seem to be at the level of organization represented by the knee-jerk, or even that represented by sensory phenomena. The disturbance appears where perceptual organization and voluntary behaviour play a role. It emerges especially in new situations where difficulty in adaptation is strikingly evident. The schizophrenic is responsive to environmental stimulation in only a superficial way, and his flow of energy into the environment is restricted unless, in some way, the environment becomes "personal."

Rabin (1944) has examined fluctuations in the mental level of 30 schizophrenics and 30 cases of other psychoses by testing, and re-testing a year later, with the Wechsler-Bellevue scales. He concludes that most schizophrenics show a rise in mental level due either to the improved clinical state or to the effect of practice. The comprehension test elicited thought-disorder to a marked degree, and so led to great fluctuations in the results.

If their test is valid, Seitz and Malholm (1947) have disproved the view that hallucinations are exaggerations of mental imagery, and, indeed, their findings suggest that deficient auditory imagery is one of the factors responsible for auditory hallucinations. A "concrete imagery" test, comprised of 120 words and phrases to which the subject responds by announcing his first mental image, was given to 40 schizophrenics, 10 patients recovered from an alcoholic hallucinosis, and 114 normal subjects. It was found that those schizophrenics who were definitely aurally hallucinated had a significantly lower mean percentage of auditory imagery than either normal subjects or schizophrenics who were not aurally hallucinated. The two last groups did not differ significantly. The recovered alcoholic patients had a significantly lower mean percentage of auditory imagery than the normal subjects, and the former did not differ significantly from the schizophrenics who were aurally hallucinated. It is,

of course, possible that the hallucinated schizophrenics were distracted by more attractive stimuli than those of the test.

Gottlieb and Coburn (1944) have studied the effects of the intravenous injection of sodium amytal along with amphetamine. Their aim was to discover definitely whether schizophrenic and depressed patients show a similarity or a difference in the development of tolerance to a combination of amytal and amphetamine sulphate. It was found that the amphetamine partially relieved drowsiness due to amytal, both in schizophrenic and depressed patients, whereas the psychological characteristics and the duration of the responses differed. In the depressed patients the psychological characteristics remained unchanged and the duration of the response was increased. In the schizophrenic patients there was a slightly poorer psychological reaction with no increase in the duration. The tolerance is understood to refer to the psychological and not the hypnotic effects. It was found that schizophrenic patients reacted with psychological responses, such as congruous affect and increased insight, which were clinically obvious in 50 per cent. of the cases. The schizophrenics had their best and longest response to the first injection, while subsequent injections on succeeding days produced poorer and shorter responses. On the other hand, patients with depressions reacted with clinically measurable responses in 90 per cent. of cases, and the rapid development of tolerance noted with schizophrenics was absent.

Huston and Singer (1945) studied the auditory reaction time in schizophrenics after intravenous injection of sodium amytal and amphetamine. The results suggested that the schizophrenics were not able to attain as high a level of mental set (attention) as normal subjects, and do not maintain their highest level as long as normal subjects. The reaction-time technique may be used to measure the improvement in attention that follows injection of sodium amytal.

Kuhn (1942) has made use of seven series of pictures from the book of a cartoonist, *Father and Son*, for testing the emotional reactions of schizophrenics. Each series depicts a story of the humorous adventures of a devoted father and his child. To each series there is a heading, but no text. In order to understand the sequence of four to eight pictures which comprises the story, a certain amount of combinatory thinking is necessary. Kuhn tested well-educated patients only and excluded cases with marked thought-disorder. The patients' responses, given in great detail, are remarkable for their lack of understanding, their inadequacy, and their numerous errors and failures. There is no attempt to assess the results in figures. The failures are explained by a defect of the emotional-cognitive functions, which is due to weakening of feelings of sympathy. In other words, empathy is impaired in schizophrenia.

Lindberg (1942) has described the application of the "Ring test" in schizophrenia. The test consists of a piece of paper divided into two fields, each containing the figure of a circle to which an arrow is attached. The circles show differences in size and form, each arrow is attached in a different position, and there are minor differences as to the location of the figure in the field, and as to the background of the circles. The two figures are given in distinctly different colours. The subject is asked to point out the differences between the two figures. In earlier work Lindberg tested 2,500 children and several

hundred adults, and found that below the age of seven years 70 per cent. of children react by pointing to the colour as main difference. With increasing age the number of colour answers diminishes, being 35 per cent. at fourteen years, and 20 per cent. among the adults. In this paper Lindberg gives the results of the test in three groups of 181 schizophrenics—one group of mild and early cases, a second of relatively quiet and accessible patients of long standing, and a third of severely disturbed, progressed cases. The frequency of colour answers increased with severity of the symptoms, and in severe schizophrenics was almost four times the average of the normals, who were surgical cases. This corresponds to a greater frequency of colour reaction to the Rorschach test in schizophrenics. The result is interpreted as a consequence of an organic disturbance of cerebral function due to schizophrenic illness, which produces a lowering of function leading to a simpler, more concrete apperception of reality.

Haffter (1946) has surveyed the different interpretations of the psychopathology of schizophrenia that have been put forward in German, Swiss and French literature since 1930. He compares and contrasts the philosophical, phenomenological, and analytical schools, but does not take sides. Optimistically and generously, he concludes that in a problem of such complexity there is justification for the various approaches.

From a patient's description of two psychotic episodes, Storch (1946) has made a philosophical analysis of schizophrenia. His approach is based on the Existentialism of Heidegger, the foremost exponent of this philosophy. Storch's paper teems with references to the early 19th century school of romantic philosophers, the forerunners of Heidegger, and to earlier mystic thinkers. The author makes many subtle observations on the psychopathology of schizophrenia, but his analysis is less concerned with clinical psychiatry than with the formation of a philosophy of life in both health and disease.

In 1942 Binswanger, one of the leading Swiss psychiatrists and philosophers, published a volume on the *Formative Principles and Knowledge of Human Existence*. Since then (1945, 1946a, 1946b) he has reported the case-histories of several psychotics and has analysed them in detail. He finds that they are perfect illustrations of certain modes of existence. He is not interested in schizophrenia as an illness or clinical entity, nor is he even interested in the psychopathology. It is as a form of mental life, of existing in the world, of managing the problems of existing, that he concerns himself with schizophrenia. He regards the individual patient as exemplifying the basic philosophical conceptions which he developed in his major publication. The case-histories give him the opportunity to discuss the problems of paranoid symptoms, their place in, and their relation to, the patient's personality and life.

CLINICAL PICTURE.

(a) *Simple Type.*

In Worcester State Hospital, Mass., Kant (1948) made a survey of all patients who had been diagnosed as simple schizophrenics. Of 741 male schizophrenics, 6.6 per cent. were of the simple type; of 679 female patients, 3.6 per cent. were of the simple type. The clinical picture differed considerably

from the textbook picture. In only two cases were hallucinations and delusions absent, and all patients had had psychotic experiences or shown greatly disintegrated behaviour. He was surprised to find that in only 20 per cent. of cases was there definite loss of contact with the environment. In 60 per cent. of patients, however, "queerness" and/or disintegration of the personality was found. In 66 per cent. of cases the illness began between the ages of 17 and 24 years. In 96 per cent. of cases the onset was insidious; in the other cases there were endocrine disorders that probably acted as precipitating factors. Only 42 cases were sufficiently documented for consideration of hereditary tainting, and 62 per cent. showed tainting with various functional psychoses of which schizophrenia was the largest group.

Personality characteristics in Kant's patients showed the following distribution: Lack of sexual adjustment (89 per cent.), lack of aggressiveness (87 per cent.), introversion (70 per cent.), desire for social contacts (65 per cent.), leptosomatic physique (60 per cent.), unreliable workers (60 per cent.), sub-normal intellectual functioning (52 per cent.).

Disintegration prevailed over withdrawal during the early stages. Disintegrated behaviour was marked in 35 per cent. of cases, delusions and/or hallucinations in 43 per cent., while withdrawal was marked in only 22 per cent. of cases. At the onset, disorder of behaviour showed the following distribution:

1. Aggression	65 per cent.
2. Sexual and alcoholic trends	40 "
3. Combination of 1 and 2	80 "
4. Combination of 1, 2 and 3, along with vagrancy	89 "
5. Hypochondriacal experiences	30 "

In 63 per cent. of cases impairment of early transference was noted and held to indicate insecurity in the family environment. In 26 per cent. of the group death of either a parent or sibling was noted during the first decade of the patient's life (*cf.* Rosenzweig and Bray, 1943). In only 3.6 per cent. of cases could the situation leading up to the schizophrenic change be said to carry unusual stress.

Kant concludes that simple schizophrenia is most characteristically schizophrenic as to heredity, pre-psychotic personality, early environment and failure to shoulder normal responsibility, and suggests that the various factors involved lead so strongly toward simple disintegration that a psychotic superstructure is not erected. Throughout his life the simple schizophrenic is in much better contact with reality than other schizophrenics. Disintegration is more basic than withdrawal, which actually may be looked on as a secondary reaction, as was suggested by the same author's work on deteriorated schizophrenics (1943). The prevalence of disintegration at all stages showed that the usual concept of simple withdrawal is superficial, and does not express the essential happening on the psychological level. In the pre-psychotic personality aggression and sexuality are frustrated, but when the simple schizophrenia breaks out they seek expression in a primitive fashion. Kant believes that the simple schizophrenic is so much more in contact with reality than most

other schizophrenics that he is less able to seek refuge in fantasy, but the converse is also possible. His material, of course, excluded the unemployables and vagrants, who are often typical examples of simple schizophrenia though they may never enter hospital.

(b) *Catatonic Type.*

For many years, and in numerous publications, Kleist and his school have attempted a subdivision of schizophrenia. It is alleged that, because of differences in clinical picture, prognosis and heredity, each sub-type can be regarded as a disease of its own, comparable with the heredo-degenerative neurological disorders.

Leonhard (1942a, 1942b and 1943) has followed his teacher Kleist in distinguishing eight forms of catatonia: akinetic, parakinetic, manneristic, iterative, negativistic, mute, cases showing automatic obedience, and hyperkinesis of speech. Typical cases, combined cases and periodic cases are also described, and Leonhard searched for and found similar clinical pictures among other members of the patient's family, especially in the periodic cases. In the minority where his search was fruitless he proceeds to assume that there must be a combination with other genetic factors, so causing different types of schizophrenia. Although the wheel has thus turned full circle Leonhard adheres to his basic conception. His views are based on small numbers of patients, and are an unfortunate relapse into a symptomatological classification that belongs to the days before Kraepelin.

While Leonhard's work aimed to prove the independence of Kleist's subgroups by demonstrating their separate genetic transmission, Neele and Kleist (1942) deal with the result of a follow-up of a small subgroup of paranoid schizophrenics which Kleist established as a separate entity more than twenty years ago. These were paranoid schizophrenics with progressive delusions of reference. Of 83 patients, 14 could not be traced, 8 had died, while 7 had been wrongly included in the subgroup. In only 20 of the remaining 54 cases was the diagnosis confirmed; the residual cases were found to belong to other subgroups of schizophrenia. In other words, only in about one-third were the ideas of reference still present at the time of the follow-up; in all others different schizophrenic symptoms had taken their place. This does not contradict his primary theory in the eyes of Kleist; he further subdivides the subgroup into patients with prevailing delusions of reference and interpretation, and patients with prevailing delusions of influence and inspiration. The age of onset for the whole subgroup he found between 30 and 44 years, with an average age of 34 years. Four-fifths of the patients were males, and they were frequently of high intelligence with good education. The outcome in a quarter of the cases was a social readjustment and discharge from hospital; but partial remissions of a limited duration were found in more than half of the cases without any of the modern physical treatments. The follow-up does support the unity of paranoid schizophrenia with the other varieties.

A new interpretation of echolalia and echopraxis in catatonic schizophrenia is given by Stengel (1947), who regards these reactions as being fundamentally social and due to an impulse to maintain some social contact in a condition

which is otherwise characterized by withdrawal. The echo-reactions in early infancy belong to a stage of development in which there still exists a confusion between "I" and "not I," and the same stage is reached in schizophrenic regression when the boundaries of the ego have broken down. To describe echo-reactions as examples of automatic obedience is only correct in a physiological sense, for psychologically the response is an ambivalent mixture of negativism and co-operation in which the negativism dominates the situation.

(c) *Paranoid Type.*

Wyrsh (1942), following up earlier studies of schizophrenic subgroups, has studied 100 unselected cases of paranoid schizophrenia in whom the psychosis had been present for two years at least. For a considerable time the patients were seen daily by the author. In 79 cases the psychosis started after the age of 30 years; against expectation 21 had become ill before they were 30. A great variety of clinical pictures is seen, but the patient's attitude towards his delusions falls into three distinct types. In the first type the patient cannot fit his delusions into his mode of life; the delusions are strange, accidental experiences which distress him. In the second type the delusional ideas are part and parcel of the patient's self; he identifies himself with them, and lives for them, although at the same time he may live an ordinary existence without any logical relation to his delusions. In the third type the patient mixes phantastic delusions with his daily life, without any clear-cut separation: both "worlds" are accepted, and neither is taken very seriously. Wyrsh proceeds to consider the problem of the cause of paranoid development in schizophrenia, but he does not decide in favour of any one general theory. He believes that the following features are important: slow development of the psychosis in a state of clear consciousness; change of general attitude to life at the beginning of schizophrenia; tendency of the patient to project and objectivate experience; certain personality features; middle age. Besides primary delusions, which can, according to the author, be understood as originating in the patient's general mood, Wyrsh regularly met secondary delusional interpretations which appear to be derived from the patient's attitude towards his pathological experiences. Wyrsh sees no possibility of separating the paranoid form from the other forms of schizophrenia. The paper is distinguished by many careful and original observations, and by the psychological acumen characteristic of the Bleuler-Klaesi school.

In 1926 Tramer published a monograph on a number of eccentric inventors. He has now (1945) followed up four of these cases, all paranoid schizophrenics, whose inventive energies were mainly directed to the problem of perpetual motion. While three of his patients had deteriorated and retained their delusions, the fourth patient was discharged from hospital after 13 years, and for the last 10 years he has been free of delusions and has adapted well to the simple life of a carpenter.

Gaupp (1942) still believes that paranoia, as defined by Kraepelin, is a separate diagnostic entity. He had published a monograph (1914) on the case of Schoolmaster Wagner. In 1913 Wagner killed his wife and four children, and shortly afterwards shot at twenty villagers, killing eight: finally he set

fire to four houses. The present paper describes in detail the similar case of a schoolmaster who murdered his wife as a consequence of a long-standing paranoid psychosis. Although the patient suffered from obvious delusions and hallucinations, and was diagnosed by other psychiatrists as a case of paranoid schizophrenia, Gaupp classifies him as a true paranoia. By minute analysis of the development of the personality, the experiences, ambitions, disappointments of his life, his sexual drives and dissatisfactions, Gaupp sees a logical and natural sequence of events leading to the psychosis, and finally to the crime. One of his principal arguments is the apparent recovery of the patient after a full explanation and analysis of his case while he was in hospital, after being relieved by the court as not responsible.

Raphael and Himler (1944) have made a study of 102 schizophrenic and 20 paranoid patients who, over a period of 12 years, came to the notice of the Student Health Service of the University of Michigan. The figures showed that schizophrenic-paranoid disorders had a higher rate of occurrence than any other psychotic reaction. Manic-depressive psychoses were a fairly close second, and both diagnoses comprised 93.9 per cent. of all psychoses noted.

The Case of Rudolf Hess, edited by J. R. Rees (1947), gives a detailed account of the psychiatric investigation of the Deputy-Fuehrer of Germany, from the time of his arrival in Scotland in 1941 until the Nuremberg trial in 1946. Psychiatrists of four nations examined Hess, and the reader will find it an instructive exercise in diagnosis to see how far he can agree with their opinions.

(d) *Schizophrenic Deterioration.*

Kant (1943), with the aid of sodium amytal, examined a group of 100 unselected male schizophrenic patients, who had been ill for at least 10 years and had remained hospitalized. The clinical pictures were analysed with reference to disturbance of behaviour and inner disorganization. By employing sodium amytal it was possible, even in highly withdrawn patients, not only to observe certain peculiarities of behaviour, but also to a fair extent to determine the state of inner organization and thus to appraise the total structure. It was found that extreme withdrawal is always accompanied by extreme disorganization. Thought disturbance of the specific type and some characteristic "queerness," expressed either in oddity of behaviour or in bizarreness of thought content, were present in each patient. The three original basic types (paranoid, hebephrenic, catatonic), to which a combined hebephrenic-catatonic type was added, were clearly delineated in the deteriorated group. Kant found that in the paranoid type there is the greatest discrepancy between the relatively slight behaviour disturbance and the high disorganization, characterized by an abundance of absurd and contradictory delusions and hallucinations. In the hebephrenic type, in which both sides of the ratios show medium and high degrees of disturbance, "queerness" is the outstanding peculiarity. The catatonics exhibit the worst reaction, combining "petrification" with an extreme degree of disorganization, expressed in complete breaking up of the thought process. Certain results of the analysis cast some doubt on the primary importance of "withdrawal," which probably has been overstressed by Hoskins

and his co-workers in the Worcester State Hospital. This over stressing occurs because, without utilizing sodium amytal, the inner disorganization frequently remains hidden behind the solely observable withdrawal. It seems likely that the latter already is the reaction to the beginning disintegration of the functioning personality, which is expressed in the disturbance of behaviour ("queerness") as well as in the inner disorganization.

In American psychiatric literature any mention of an organic approach is usually timid and prefaced by an apology. It is therefore refreshing to read the work of Arieti (1944a, 1945a and 1945b), who believes that valuable information may be obtained from the study of advanced cases of schizophrenia. He describes preterminal and terminal stages. The former begins 5 to 15 years after the start of the illness, at a time when thinking is disintegrated and hallucinations and delusions are about to disappear, or are unsupported by affect. In this stage self-decorating and hoarding are prominent. Arieti believes it is profitable to consider these habits from a psychoanalytic standpoint (regression of libido), and also from the standpoint of Hughlings Jackson (release of evolutionary levels). He regards the terminal stage as starting when the decreased activity of the deteriorating schizophrenic is replaced by a fairly sudden increase in motor activity which tends to be lasting. The patients no longer seem able to experience hallucinations or to elaborate delusions, and their verbal expressions are much reduced. At this time bulimia and grabbing of food become prominent, and may later be replaced by the "placing into mouth" of all sorts of inedible objects. The seemingly compulsive "placing into mouth" can be observed in 2-year-old children, in cats and monkeys who have had both temporal lobes excised, and in some cases of Pick's cortical atrophy. At a still later stage in schizophrenia insensitivity to pain, temperature and taste appears, although olfactory sensation remains intact. The author does not believe that the real sensations of pain and temperature are lost, but considers the perception of the stimuli is impaired. He agrees that the impairment may be due to apathy, but prefers to think the disorder is an agnosia, or "psychic analgesia."

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS.

K. Schneider (1942) has arranged schizophrenic symptoms in two groups according to their value in diagnosis. He thinks that the diagnosis may be definitely made if the patient (a) has primary delusions; (b) hears his own thoughts spoken aloud; (c) hears voices conversing together; (d) hears voices which remark on the patient's actions at the time; (e) has tactile hallucinations, such as sexual hallucinations; (f) has passivity feelings as to emotions, impulses and volition, or feels that ideas are taken away, or otherwise influenced. In the absence of a symptomatic psychosis these symptoms are considered diagnostic, although they are not always readily identified. In the second group Schneider lists symptoms that are not so characteristic, and includes hallucinations, thought-blocking, incoherence, perplexity, compulsive symptoms, depersonalization, depression, and subjective impairment of feeling. Often the diagnosis has to be made from these symptoms, though they are not firmly diagnostic unless the whole clinical picture is schizophrenic.

Weitz (1947) has made a search for schizophrenic symptoms in symptomatic, toxic and organic psychoses. He perused the case-records of 1,930 such patients for the presence of Schneider's symptoms of the first group and found them in 9 cases only—in 4 cases of G.P.I., 1 of cerebral arteriosclerosis, 1 of disseminated sclerosis, 2 of alcoholic hallucinosis, and 1 of epileptic twilight state. Even if those who wrote the case-records had overlooked some symptoms, Weitz's results support the specificity of the symptoms, and oppose the views of Manfred Bleuler (1948a) and others who believe that the psychological pictures of schizophrenia and of symptomatic psychoses may be indistinguishable.

To aid in the differential diagnosis between schizophrenia and psychogenic psychosis, Faergeman (1946) has made a statistical investigation into the relative diagnostic importance of psychic trauma, affective intensity, presence of hallucinations, duration of the illness beyond three months, and paranoid delusions. To each of these factors a positive or negative points value is given, and he considers that all cases with a points value of more than + 30 are psychogenic psychoses, and those under - 43 are schizophrenics. In his material, 71 per cent. of the patients subsequently shown to have psychogenic psychoses had values above + 30, and 51 per cent. of verified schizophrenics had values below - 43. The author does well to stress that the method depends ultimately on clinical assessments.

Polatin *et al.* (1944) point out that although organic psychoses usually offer no difficulty in diagnosis when disorientation, disturbance of memory or other gross sensorial defects appear, yet difficulty is encountered when patients show bizarre behaviour and are mute or otherwise inaccessible to testing. Psychiatric examination and Rorschach testing after intravenous barbiturates, air encephalography, examination of the cerebrospinal fluid, biopsy of the brain and electroencephalography may demonstrate organic brain disease. Two case-histories are given: seclusiveness, catatonia, emotional blunting, paranoid delusions and hallucinations led to the diagnosis of schizophrenia, which had to be revised when the above investigations demonstrated cortical degenerative disease.

From his experience as a psychiatrist in the Royal Navy, Garmany (1946) has emphasized how schizophrenia in its early stages often presents with symptoms of anxiety, depression and hysteria, or with minor delinquencies of a speciously psychopathic nature. He found no evidence to suggest that personal stress during Naval service would precipitate schizophrenia which would not otherwise have appeared.

De Jong and St. John (1945) refer to a possible liver pathology as the basis for catatonic schizophrenia, and give a report of the cephalin-cholesterol flocculation test of liver function. It is well known that tests of liver function give varied and unreliable results even in cases with known liver damage. De Jong and St. John report a very small series, and not even all their few catatonic cases gave positive results; nevertheless they suggest that the test may help in the differential diagnosis of certain cases of catatonic schizophrenia. Zimmermann *et al.* (1948) have employed the test routinely since 1945 on all admissions to the Colorado State Hospital, and of 175 consecutive admissions

that were later diagnosed as schizophrenics, none of 96 males and only 5 of 79 females gave positive results. In a mixed non-schizophrenic group of 210 cases, 6 males and 7 females gave positive results. No positive results were found in 22 recent cases, nor in 12 established cases of catatonic schizophrenia. Speijer (1948) had similarly disappointing results. He tested 261 schizophrenics and 265 controls. No differences were found between the two groups, and even fewer positive reactions in catatonics than in the other types of schizophrenia. More positive reactions were found with both schizophrenics and control groups in women than in men, but the difference was not significant. It may be concluded that the test is of no value in schizophrenia.

COURSE AND PROGNOSIS.

In a paper read in June, 1947, to the Vienna Society of Psychiatry and Neurology, Manfred Bleuler (1948a) has expressed his present views on the problem of schizophrenia. After a brief historical survey, he states that the many expectations that were raised by the work of Kraepelin and Eugen Bleuler have not been fulfilled. The concept of schizophrenia has become rigid, and we still do not know if what appears to be a symptomatological entity is also a genetic entity. He believes that the hallucinations, thought disorder, passivity feelings, emotional disorder and the motor symptoms are only varying aspects of the fundamental schizophrenic disorder. Psychopathological study of the symptoms has made it possible to draw a line between schizophrenia and the organic psychoses because the psychological symptoms are quite different. However, the lines of demarcation between schizophrenia and manic-depressive psychosis, and between schizophrenia and symptomatic psychoses, are ill-defined.

Bleuler's own studies on 500 patients who were followed up for 15 years give, he thinks, a clearer picture of the course of schizophrenia than has hitherto been available. All but 5 per cent. of his cases showed one of seven types of clinical course:

- | | | |
|--|-------|----------------|
| 1. Acute onset leading to dementia | . . . | 5-15 per cent. |
| 2. Insidious onset leading to dementia | . . . | 10-20 " |
| 3. Acute onset with later arrest of the illness and resultant personality defect | . . . | less than 5 " |
| 4. Insidious onset with later arrest of the illness and resultant personality defect | . . . | 5-10 " |
| 5. Periodic course ending in dementia | . . . | 5 " |
| 6. Periodic course ending in personality defect | . . . | 30-40 " |
| 7. Periodic course ending in recovery | . . . | 25-35 " |

These figures are the limits found in different localities and under different circumstances, and they do not include patients who have never been in hospital. As a rough guide, it may be said that a quarter of all cases end in severe deterioration, a second quarter end in marked personality defect, a third quarter end in mild personality defect, and the fourth quarter recover.

Bleuler finds that a periodic course is rather more frequent than a simple

progressive course, and the periodic cases rarely end in severe dementia. Most cases having an insidious onset end in severe deterioration, and recovery is exceptional. Of those cases having an acute onset only a quarter end in severe dementia; a quarter recover, and the remaining cases end up with a more or less severe defect of personality. In view of Bleuler's reluctance to draw a firm line in the differential diagnosis of schizophrenia from manic-depressive psychosis, it may be suspected that in his large fraction of periodic cases there is included a number of patients whom other observers would regard as manic-depressives. If the figures can be confirmed, however, it is unnecessary to stress how important they will be for those who are attempting to assess the value of the modern physical treatments.

Tangemann (1942) has reported a follow-up study of 418 cases of schizophrenia. The spontaneous remission rate was assessed so as to provide a control series for comparison with cases receiving the modern physical treatments. Eighty per cent. of the patients were followed up for more than five years, and the total percentage of social remissions was only 18.2. Neumann and Finkenbrink (1939), and Hutter (1941), found respectively 32.9 and 32.3 per cent. social remissions. Hutter agrees with Tangemann that catatonic cases have the best prognosis, and are surpassed only by cases with an admixture of manic-depressive features. The latter worker found that the prospects of a lasting remission were greatest during the first two years of illness, and that after the illness had lasted five years prospects were negligible. He found remissions in 52.5 per cent. of his patients who had a duration of illness under one year, and in 47.1 per cent. of his patients whose illness had been present less than two years. His material included 206 patients whose course was periodic, consisting of a series of attacks followed by either complete or incomplete remissions. Lasting remissions took place in 65 per cent. of patients who had had one attack, in 22 per cent. of patients who had had two attacks, and in very few patients who had had three attacks. Although these figures show the need for early treatment, the results are based on small series of patients in each group and the usual statistical corrections are not applied. Tangemann has also studied the physical constitution of 218 of his cases, and finds the tendency to remission is greatest in pyknics and least in dysplastics (see table). He found that a pyknic physique was commoner in those schizophrenics whose illness began late in life than in those starting in youth.

Physique.	Number of cases.	Number of remissions.	Percentage of remissions.
Leptosomatic .	147	33	22.4
Athletic .	38	15	39.4
Dysplastic .	12	1	8.3
Pyknic .	21	12	57.1

Hedenberg (1943) finds that in those schizophrenics who fall ill early in life the course is severe and deteriorating, whereas when the onset is late in life a mild personality defect is common. He believes that the brain of the middle-aged person reacts to the schizophrenic noxa (whatever that may be) in a different manner from that of the more sensitive juvenile brain.

Danziger (1946a) has used data of the U.S. Bureau of the Census to prepare tables which show the schizophrenic patient's prospect of being discharged improved or recovered from American State Hospitals when no shock treatment is applied. The chance of recovery is very small after two or three years in hospital, but there is some prospect for improvement even after ten years' hospitalization.

Wyrsch (1941) examined 26,000 case-records in order to collect cases which had had a remission lasting not less than fifteen years. It was his aim to determine if a separate sub-type was involved, but although he discovered 57 such cases he was unable to delineate any sub-type.

Kant (1944) has elaborated on his well-known studies of recovered and deteriorated schizophrenics. He stresses that in prognosis, as in diagnosis, the whole clinical picture should be viewed; for instance, affective blunting or disordered associations have little meaning apart from the general structure in which they appear. This leads to the author's axiom that in schizophrenia the prognosis is worse the more fundamentally schizophrenic are the clinical picture, the pre-psychotic personality and the hereditary loading. He regards as benign clinical pictures those (1) in which clouding of consciousness prevails during the whole course; (2) associated with clear consciousness in which the more schizophrenic-appearing symptomatology, such as paranoid experiences, hallucinations, resistiveness, posturing, etc., are related to a manic or depressive element; (3) in which there are alternating states of stupor and excitement with fragmentation of mental activity, provided these states are not associated with malignant features. Malignant pictures are those characterized by the predominance of direct process symptoms, and hence by lack of uniformity. Thought disorder is the one feature which all chronic schizophrenics have in common.

TREATMENT.

Insulin coma treatment, convulsant therapy and leucotomy operations are described in separate chapters. Jostling in the rear of these established therapies come all sorts of modifications, some based on empiricism, and others derived from more or less careful considerations. Even these last, such as the malononitrile therapy of the Stockholm school, produce results that compare unfavourably with those of the empirical methods.

(a) *Physical Therapy.*

Proceeding from their finding that malononitrile increases nucleoprotein production in rabbits, Hyden and Hartelius (1948) have investigated the therapeutic effects of intravenous injections of 5 per cent. malononitrile (1-6 mgm. per kgm. body weight) in schizophrenic and manic-depressive patients. The malononitrile is allowed to act for 30 to 60 minutes, and is then counteracted by the intravenous injection of 5 per cent. sodium thiosulphate. The treatments are given two or three times a week, and a course consists of from 6 to 15 treatments. In schizophrenia, malononitrile causes an initial exaggeration of autism and catatonia, which are followed, in responsive cases, by increased contact, affectivity, coherence and improved sleep. The beneficial effects are most obvious the day after treatment and, as with E.C.T., may persist and be

augmented until a remission is produced. As the treatment is simple and comparatively free of complications thorough testing of its potentialities is indicated, although the authors claim only five lasting improvements out of 15 cases treated.

Schottky (1943) observed a catatonic patient who refused most foods, but greedily swallowed everything rich in carbohydrates. With a faith in the *vis medicatrix naturae* that is unusual in German students of schizophrenia, he devised a therapeutic diet devoid of animal protein. After purification of the bowel by enemata he gave a diet rich in carbohydrate, vegetables, and fruit, but with only small amounts of fat. Ample fluids were given containing 100 gm. of glucose per day. Ascorbic acid, aneurin, nicotinamide and lactoflavin were given in large doses on alternate days. The regime was followed for two weeks, during which time the patient was carefully nursed as though he were physically ill. In chronic cases the results were poor, but Schottky claimed marked improvement in acute catatonic excitements of early schizophrenia which had not responded to insulin coma and E.C.T.: agitation and insomnia lessened and the patients became accessible. In addition there was a concomitant improvement in physical condition resembling that in the patient who is convalescing from a severe physical illness. It was Schottky's impression that he was witnessing a detoxicative process. Unfortunately he gives neither statistics nor case-histories, makes no mention of controls, and does not seem to have heard of Gjessing's work.

Lofvendahl and Arnoldi (1945) have given a preliminary report of a similar attempt to effect improvement in chronic schizophrenics by dietetic measures. The work proceeds from Gjessing's investigations of nitrogen metabolism in periodic schizophrenia, and also from a patient's announcement that her periodic attacks were favourably influenced when she lowered her intake of meat and raised her intake of potatoes. The authors aim was to diminish the nitrogen intake and increase the nitrogen excretion. A diet low in protein and fat and rich in carbohydrates was given. Carbohydrate metabolism was stimulated by vitamin B and insulin, while alkalis were administered to remove acid metabolites. After two weeks of this regime it was found that the serum nitrogen and the urine nitrogen became lower. In the small series treated there was a general impression of clinical improvement.

The "vascular shock" treatment by acetylcholine, introduced by Fiamberti (1939), is still popular in the land that saw the birth of E.C.T. Cohen *et al.* (1944) report on a paranoid schizophrenic who remitted fully after his fourth acetylcholine treatment, although his seven-month-old psychosis had not responded to 24 electric convulsions that were given initially. It happened, however, that during the fourth acetylcholine treatment the patient was comatose for an hour, during which time he became pulseless for up to two minutes. The authors do not report their case from any satisfaction with the treatment, which they believe to be dangerous and unjustified. They assert that their one recovery was an example of their experience with other shock treatments, namely, that brain damage, reversible or irreversible, is the basis of the clinical improvement. They suggest, somewhat cynically, that this brain damage acts in a way similar to that of the progress of the schizophrenic

disease, namely, that the patient is no longer sufficiently intact to react with florid, productive symptoms.

In order to evaluate the effect of depression of brain metabolism without any direct stimulatory effects on the brain, Bellinger *et al.* (1943) subjected patients with schizophrenia to nitrogen inhalation therapy. Sixty-five patients ill less than one year and 34 ill for more than one year were treated. Of the patients ill less than one year, 46 per cent. were improved and 34 per cent. paroled. Of those ill longer than a year, 34 per cent. were improved and 9 per cent. were paroled. From an analysis of these results, and a comparison with those obtained by other treatments, the authors conclude that depression of brain metabolism exerts a desirable effect on the course of schizophrenia, that the duration of depression is of importance, and that in the treatment of schizophrenia, the longer periods of depression produced by insulin coma are more valuable than the shorter ones caused by nitrogen inhalation or cardiazol. On the other hand, Danziger and Kindwall (1948) assume, on theoretical grounds, that mental disorder is due to depression of brain metabolism and cerebral anoxia. They have treated 13 established schizophrenics, and 11 other psychiatric patients, with thyroid in doses of 2 to 8 grains per day for many months. All the schizophrenic patients recovered: 4 of them had thyroid and vitamin B alone; 9 received E.C.T. and insulin coma treatment as well. The aim of the treatment was to raise the B.M.R. from a low, or low normal, value to a high normal value. Weights tended to become normal, and no serious toxic symptoms occurred.

Pfeffer and Pescor (1944) have given multiple blood transfusions because of the possibility that schizophrenia is due to a faulty metabolism of the brain cells, either because of a lack of certain essential substances, or because of the presence of toxic products which interfere with metabolism. This naïvely logical treatment was given to six patients: the donors were non-psychotic, narcotic addicts without "active habits." From one-half to one litre of blood was withdrawn from the schizophrenic patients, and a similar amount of donor's blood was transfused. In five of the six cases the donated blood was of the same group as that of the recipients, and about six transfusions were given over a period of seven to ten days. Only one of the six patients showed significant improvement, and the authors concluded that this remission could be accounted for by a spontaneous remission, by the additional nursing attentions, or by the pyrexia following the transfusions.

Cobb (1947) quotes the claims of Russian psychiatrists that considerable improvement in schizophrenia results from haemocolloidoclastic shock which involves the intravenous injection of 5-35 c.c. of incompatible blood. The treatments are given twice weekly for a month, and excite an immediate disturbance of vasomotor and vegetative functions and a pyrexia of 104° F. Fuster (1944) induces electrical convulsions whilst the patient is undergoing a period of pyrexia produced by a chemical pyrogen, an aqueous suspension of colloidal sulphur. Twenty patients received the treatment twice weekly for a month, and seven cases showed definite improvement. These seven had previously shown slight temporary improvement following cardiazol and E.C.T., but insulin coma treatment had had no curative effect.

Ivanov-Smolenski (1946) follows Pavlov in attributing schizophrenia to inhibition of the cerebral cortex. Because of this hypothetical inhibition he has used prolonged narcosis combined with measures to stimulate the vegetative functions. He thus combines sodium amytal narcosis with sulfosin fever therapy, with chemical convulsant therapy, and with modified insulin therapy. He claims 70 per cent. remissions in cases which have been ill less than one year. He believes that the most useful treatments, insulin coma therapy, convulsant therapy, and deep narcosis, have in common a diffuse inhibition of cortical function and stimulation of the hypothalamic, diencephalic and vegetative centres. In using his various combined methods the author claims that he obtains better results, with fewer risks, than by any of the three methods used alone.

Hemphill and Reiss (1948) cite the interesting case of a chronic catatonic whose total ketosteroid excretion was normal in amount, but who excreted no dehydro-androsterone. Following treatment with testosterone he achieved a partial remission, which was maintained as long as testosterone was exhibited.

Over the years, Loewenstein (1945) has found tubercle bacilli in the cerebro-spinal fluid of schizophrenics with a frequency that is equalled by the failure of other workers to confirm his findings. He believes that convulsive therapy effects improvement by dislodging bacillary thrombi from the small cerebral vessels. To disperse these thrombi, he has evolved an ingenious treatment (1944) whereby the blood pressure is lowered by the inhalation of amyl nitrite, and then raised by the intravenous injection of adrenalin.

Kalinowsky and Putnam (1943) have found that Dilantin (Epanutin), in large doses diminished excitement and irritability in schizophrenia and other psychoses. Hall (1948) has found similar beneficial effects from the exhibition of Tridione.

(b) *Psychotherapy.*

Group psychotherapy has been studied by Kraupl (1947). Two types of group were organized: the first was made up of four schizophrenic and four neurotic patients; the second was composed mainly of schizophrenics and was usually larger. The patients repeatedly discussed their own symptoms, sex outlets, feelings of inferiority and aggressive trends. Sometimes the discussion stirred up emotional conflicts which led to aggressive conduct both within and outside the group. Just as in individual psychotherapy, it was found that the therapist became the object of transference reactions. The reticence shown by schizophrenics during an individual interview often became less in the group, apparently because of the tolerant attitude of the group members; thus patients revealed themselves openly. Kraupl found that homosexual tendencies were aroused by the group situation but were fairly easily socialized. Dominant personalities arose in each group, but the qualities that made for dominance were difficult to determine, though superior intelligence, verbal facility, exhibitionistic trends and single mindedness were probably factors. In this preliminary study Kraupl did not feel justified in commenting on therapeutic effects. Favourable results have been reported, however, by Foulkes and Lewis (1944), while Stengel (1948) found group therapy particularly helpful with patients who were about to remit. Stengel noted that the patient's

reaction to the group situation contributed to an assessment of the degree to which the social personality was preserved.

Overholt (1947) has described the psychotherapeutic approach he employs towards "ambulatory schizophrenia." Although the author perhaps believes himself reactionary for confessing that he does not consider organic factors to be unimportant, his supportive psychotherapy is undoubtedly of the greatest help to accessible schizophrenics. He says that in psychotherapy a secure relationship between patient and therapist is always essential, but that its attainment in schizophrenia is more difficult than in other mental illnesses. The therapist must accept the patient as a fellow human rather than as a creature of another world. This acceptance is not readily achieved, because the therapist is often unconsciously blocked by the very process of his own adjustment to a world which the schizophrenic has relinquished. The author's method is derived from the psychoanalytic approach, but there are important differences in the depth, intensity and goal of treatment. The treatment is based on the concept that the schizophrenic is a lonely isolated individual who is seeking acceptance and understanding. Few will dispute Overholt's opinion that schizophrenics of this group benefit surprisingly from such psychotherapy.

Wyrsch (1945) has discussed the field of psychotherapy in symptom-poor schizophrenia, and points out how interpretation and analysis are hardly possible because of the paucity of symptoms, and because there is little or no reaction to such symptoms as are present. There are, however, some patients who are distressed by their primary schizophrenic illness and who do seek treatment. Such patients may be taught to be objective, and may gain a perspective of themselves and their illness if they can be made to recognize their subjectively experienced disturbances as being psychopathological symptoms. Apart from the peace of mind they acquire, the appearance of secondary symptoms may be prevented and psychotherapy becomes possible in the narrow sense.

Psychotherapy, in the broader sense, is advocated by Rosen (1946), who applies certain basic psychoanalytic concepts in order to penetrate acute catatonic psychoses. Impressed by the fear which is often marked in such psychoses, Rosen assumes the identities of the figures threatening the patient, and reassures him that, far from meaning harm, these figures would rather love and cherish him. Rosen stayed with his patients for periods up to 16 hours, and did not leave them until, presumably because of physical and mental exhaustion, they calmed down. Although the author might not concur, this treatment should perhaps be classed with the physical shock therapies. Writing a year later, Rosen (1947) describes, with one case-history, how he has cured 36 out of 37 so-called deteriorated schizophrenics by direct analytic therapy. The method consists of the therapist conversing with the patient in the language of the unconscious. These talks are, of course, time-consuming: in one case of catatonic schizophrenia Rosen tended, fed and treated the patient like a baby for 9 months. During 2 of these symbolic months he spent 10 hours a day with her, and for the remaining 7 months he spent 4 hours a day. The reader need not be accused of scepticism if he recalls that there is a strong

tendency to spontaneous remission in acute catatonia, and that individual attention and stimulation will improve many schizophrenics.

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PROBLEMS OF OLD AGE AND THE SENILE AND ARTERIOSCLEROTIC PSYCHOSES.

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I. THE BIOLOGY OF OLD AGE.

IN few branches of psychiatry are the biological, social, psychological and pathological factors so closely intertwined as in the mental disorders of old age. In each case of mental illness in an elderly person we deal not merely with the effects of demonstrable pathological lesions in the brain, as Rothschild and other American authors have recently pointed out, but with the individual personality who has suffered the damage, as well as with the cultural milieu which dictates whether in old age he is a Chinese patriarch playing an active and respected role in the life of society, or one of those lonely old people in a large modern city struggling to maintain a precarious existence. Also within the complicated causal nexus is the "age-specific decline of our faculties" which decides in some as yet unknown manner that an illness, reversible in youth, proves fatal in old age. It is, therefore, only against a background of present-day social and biological orientations towards the problems of old age that the more specifically psychiatric contributions can be evaluated.

The diverse accounts of senescence have drawn upon a variety of biological processes and events for their theme. Endocrinologists would, with some justice, name the climacteric as the starting-point of the ageing process. Psychologists, on the other hand, point to the peak reached by most individuals in their performance in tests measuring intellectual and physical prowess at about the age of twenty-five. The gradual decline that follows must surely parallel the ageing process. There is no good reason, however, why the age of ten, when hearing is at its most sensitive for higher frequencies (Koga and Morant, 1924) should not be named as the starting-point. Nor would it be less logical to side with Minot (1908), who, by using rate of growth as measure of vitality, showed that ageing proceeds continuously throughout life. As for the relative decrease in weight of organs, said to be an accurate indicator of ageing in rats (Korenchevsky, 1949), we may be certain that when it has been fully worked out for man it will give us yet one more version of the ageing process. An interesting speculation has arisen from Simms' (1946) use of the logarithmic increase in mortality from various types of disease process with age, to depict senescence. He shows that from the age of about ten there is a gradual increase in mortality. The mortality from most infections, for example, rises by about 5 per cent. with each year of age. If mortality could

be maintained at the figure for the age of ten he estimates that man would have a life expectancy of eight hundred years!

Given the fact that decrepitude is the inexorable fate of the chronologically old, it is easy to see why evolution should eventually chance on some neat method, such as "natural death," to dispose of them as soon as they are burdens rather than assets to the species. Medawar has pointed out, however, that theories such as that of Weissmann based upon the evolutionary "utility" of death assume most of what they set out to prove. Selective advantage is conferred on a species by elimination of the old only if they are decrepit. It is this decrepitude that requires explanation, for in animals such as fishes and insects with little or no morphological evidence of ageing at death, the old, far from being a burden to the species, presumably have a richer store of antibodies as well as experience than the young. In a stimulating essay Medawar (1946) has successfully integrated facts such as these into an interesting hypothesis about the biological derivation of senescence. He makes the starting-point of his argument an hypothetically immortal population in which neither vitality nor fertility decreases with chronological age. If a number of causes of death of random incidence were superimposed upon such a population, certain effects upon its age distribution would follow. Each generation, having been exposed to the chance of random extinction more often than the preceding one, would be correspondingly reduced in numbers by a fixed ratio. Eventually a state of equilibrium would be reached in which time and the chances of accidental death would remove individuals from an age group at the same rate as they were being fed into it. The curve representing the age distribution of this population would be of the "exponential die away" type. Medawar suggests that the process of senescence has been genetically moulded to a pattern set by such an immortal age distribution. For the numerical advantage of the young would ensure that genes favouring them at the expense of the old must spread more rapidly through this population than those with an opposite effect. If a decline in fertility with age should develop as a result, advantageous genes expressed some time after birth would henceforth tend to have their age of manifestation pushed towards youth, while the converse would hold for genes with unfavourable effects. The selective advantage of the young over the old would be further increased by the slower elimination of disadvantageous mutants expressed in later age groups. For the later in life a gene causing physical or mental impairment is manifested, the less its effect on the fitness (i.e. number of offspring) of individuals whose fertility declines with age. Thus, in such an hypothetically immortal population the chronologically old would in due course become physiologically decrepit also, as a result of the action of natural selection.

We are beginning to acquire an insight into some of the essential features of this decrepitude. It is not a fate one would have predicted for organisms from a study in isolation of the individual cells of which they are constituted. Though slow in commencing to grow in tissue culture, old cells show the same capacity as young cells for exceeding the life-span of the parent organism (Medawar, 1942). On the other hand, there is evidence to suggest that humoral factors may play an important part in the causation of cellular ageing. Thus

tissue fluids from a young animal enhance the growth in culture of cells from an older one. Some of the possible humoral components concerned are suggested by the work of Thomson (1949). He has shown that there are consistent changes in the blood chemistry of apparently healthy old men; the sodium and chloride are reduced, the hypoglycaemic response to intravenous insulin is decreased, storage of vitamin C is defective and the excretion of 17-ketosteroids is diminished. He is inclined to attribute the changes to a deficiency of the suprarenal cortex, and he has shown that they may be reversed by injections of testosterone. Other biochemical and physiological changes have been described (Stewart, 1947). Among them are diminished glucose tolerance, decreased plasma protein, an increase in the E.S.R., altered permeability at cell surfaces and a reduced B.M.R. To these may be added impaired regulation of the pH of the blood, progressive loss in efficiency of temperature control, reduction in excretory ability of the kidney, and a diminished resistance to infection, this last suggested by animal experiments to be due to a fall in the level of antibodies, agglutinins and precipitins in the blood (Shock, 1945). Summarizing our knowledge to date of the physiological aspects of old age, Shock suggests that most of the phenomena of ageing may be attributed to a loss of homeostatic capacities in the organism. Regulation of the internal environment in the aged requires the use of the reserve capacities rarely invoked in younger people. Mental diseases form no exception to these rules, but social as well as physiological factors may play a part in the breakdown of homeostasis.

Research into ageing is hindered by the fact that the contribution of pathological processes of exogenous origin is difficult to disentangle in senescence from genetically determined factors, and from the rather more hypothetical component of "internal metabolic breakdown," which is possibly peculiar to a systemic organization of interacting and interdependent cellular tissues as distinct from isolated cells in tissue culture. Since the last two are made overt partly because they produce an increased vulnerability to exogenous noxae, it follows that any sharp line of demarcation between the physiological and pathological components of the ageing process must be arbitrary as well as artificial. In combating hypertension, endocrine deficiency and intellectual deterioration we may be dealing with extrinsic or genetic effects, probably both. It has been suggested, therefore (Korenchevsky, 1942, 1949), that we should proceed in an empirical manner, and that the treatment of deficiencies, infections, etc., in old age should be carried out on a large scale. The results of clinical trials of this kind reviewed by Korenchevsky in 1942 were, however, disappointing on the whole.

Attempts to influence ageing, of greater theoretical interest, made by McKay and his associates, have recently been followed up (Saxton, 1945). It has been shown that not only does restriction of calories in an otherwise adequate diet significantly increase the life-span of rats, but it also inhibits the development of inflammatory, neoplastic and degenerative diseases common in rats in old age. Saxton emphasizes the importance of these observations in view of statistical proof produced by Tannenbaum (1940) that human beings who are overweight are especially prone to develop tumours, and of the well-

known association of obesity with an increased frequency of disease and a decreased life expectancy.

2. SOCIAL ASPECTS AND STATISTICS OF OLD AGE MENTAL DISORDER.

During recent years the problems consequent upon the ageing of the population in all countries with an urban civilization have to an increasing extent engaged the attention of psychiatrists in common with workers in other fields of medicine. Advances in prophylaxis and therapeutics are providing an ever more efficient guarantee of survival to old age. In none of the major industrial countries with the possible exception of Soviet Russia is there a birth rate adequate to keep pace with the resulting increase in the number of the aged, so as to prevent a steady rise in their relative proportions in the population.

In Great Britain the number of men and women of sixty and over increased from two and a half to six and a quarter million between 1910 and 1942 (Warren, 1946). In the forty years to 1940 the total population of the U.S.A. increased by 73 per cent., but the over sixty-fives increased their numbers by 192 per cent. If the trend represented by these figures should continue unchanged the figures in 1980 for the U.S.A. will be 21 per cent. and 105 per cent. respectively (Johnson, 1946). The general social implications of these facts are grave. Unless the population trends are reversed, or the old permitted to make a more positive contribution to the social and economic life of the community, an increasing number of people will become dependent on a shrinking employable population of under-sixties. Some of the possible social and economic repercussions have been described by Frank (1946).

The facts are, however, of special significance for psychiatry, since many features of the urban civilization of countries such as Great Britain and the U.S.A. operate with a preferential severity against the old in a way conducive to mental illness. Intense competition in which a premium is placed on speed as opposed to skill and experience often deprives them of economic independence (Dunham, 1945). With the break-up of the old pattern of family life in overcrowded cities the aged, now an economic burden rather than objects of family pride, are forced to live lonely, passive, insecure and dependent lives, to which their adjustment is necessarily precarious. It is against a background of such facts that the recent statistics of mental disorder in the old should be examined. The possible effect of the ageing of the population upon the future incidence of old age psychosis has been investigated by a number of authors. Analysing the trend in first admissions to mental hospitals in England and Wales in different age groups, A. Lewis (1946) calculated that by 1971 the number of persons over forty-five admitted in a first attack will be sixteen thousand—that is, only three thousand less than the total first attack admissions for all mental illnesses in 1937. The number of patients over sixty-five admitted for the first time will be six thousand. These figures were derived from the Registrar-General's admittedly conservative estimate that persons over sixty-five will form 17 per cent. of the population by 1971.

If American figures are to be taken as a guide, it would seem unwise in calculating future trends to assume that the proportion of the aged becoming

mentally ill will remain constant. Pollock (1945) has shown that the rate of incidence of senile psychoses in New York State doubled between 1920 and 1942, while that for arteriosclerotic psychosis was multiplied by four. He quotes corresponding figures from other parts of the country. The increase in the senile group could be accounted for by the growth and ageing of the population in the intervening years, but this explanation was inadequate to explain the vast increase in arteriosclerotic psychosis. Malzberg (1945) calculated that the expectation of this disorder in New York State had increased from 51.2 to 113.9 per ten thousand for males between 1920 and 1940, and from 37.4 to 186.3 for females. He rejected a more enlightened attitude to hospital admission as an explanation, since admission rates for other psychoses had decreased in the same period. However, this does not exclude the possibility that families had become more prone to unburden themselves of aged psychotic relatives in particular. In one hospital in Pennsylvania the rate of admission of patients over sixty-five had more than doubled between 1910 and 1944. Johnson (1946) shows that this increase in rate of admission far exceeds the rate of increase of this age group in the general population. He predicts that within a decade senile and arteriosclerotic psychosis will relegate schizophrenia to second place in number of new admissions, and advocates the establishment of a geriatric unit in every mental hospital to lend new dignity to the work of caring for the older psychiatric patients. Such a unit could undertake research and help to establish a positive attitude towards the problems of psychiatric disorder in old age. Adequate plans must be made now, he believes, to meet the increasing influx of old patients, otherwise programmes for the active treatment of younger patients which have transformed the atmosphere of mental hospitals in recent years will be disorganized.

The glaring discrepancy between these figures showing a vast increase in the incidence of senile and arteriosclerotic psychosis in America in recent years, and those for England and Wales, which showed a decline (uninterrupted in the case of males) in the admission rate of patients over sixty-five between 1907 and 1937, was noted by Lewis (1946). He quotes evidence suggesting that the British figures may understate the incidence of old age psychosis because many cases relevant to the statistics are accommodated at public assistance institutions. That the number of mentally sick in institutions of this character is in fact considerable is also suggested by the observations of Affleck (1948). He found that 37 per cent. of patients admitted to hospitals for the chronic sick suffered from concomitant or uncomplicated mental illness. This is a remarkable figure, considering that it does not include milder cases of senile dementia with forgetfulness, emotional restriction and narrowing of interest. However, there is no clear evidence that such figures represent an increase on those in former years. Moreover, even if the number of mentally diseased aged in institutions other than mental hospitals could be conclusively shown to have increased significantly, it would seem at least doubtful if this would suffice to transmute the decrease in old age psychosis portrayed by the British figures into the increase reflected by those from America.

There are some indications that, as Lewis suggested, some of the causes for the discrepancy may reside in certain social and economic differences

between the two countries. The period covered by Lewis's survey is 1907-1937. 1908 saw the introduction in this country of non-contributory old age pensions, while in 1911 the National Insurance Act made a beginning of insuring against ill-health and unemployment. Between 1914 and 1938 the numbers covered by health insurance grew from thirteen to twenty million, old age pensioners from 800,000 to 2.5 million (Abrams, 1945). In the U.S.A., on the other hand, unemployment insurance was not provided for on any scale until the Federal Social Security Act of 1935. Judged by British standards the benefits prescribed by this Act were exiguous. According to Dewhurst *et al.* (1947) the proportion of old men gainfully occupied has declined from three out of four men 65 years old and over in 1890 to less than half in 1940. It would seem, therefore, that this absence of insurance against unemployment may well have been a cause of economic insecurity operating with especial severity in the case of the aged. Old age pensions (unlike those in this country, for superannuated workers only) were established in 1935 by the same Act, but Kuczynski has quoted the number of people receiving old age assistance in 1943 as being only 2.25 million. The number of people over sixty-five in the U.S.A. at about the same time was nine million (N. Lewis, 1945).

The suggestion offered by these figures when considered in conjunction with those quoted above for old age psychosis is that the less adequate the protection of the old against social insecurity the higher the overt incidence of senile mental illness. It will be remembered that in the famous survey conducted in Chicago by Faris and Dunham in 1939, the findings pointed in the same direction. Dunham (1945), restating some of his conclusions in a valuable essay on "Sociological Aspects of Mental Disorders in Later Life," said: "This ecological study points to the fact that older people in a poverty situation and in communities of disorganized family life are more likely to be identified as psychotic cases than those older persons who live in more acceptable economic surroundings and still enjoy a fair degree of familial support." Dunham also gives figures illustrating the low admission rate of old age psychoses in rural as opposed to urban areas. He contrasts the unhappy precarious plight of the aged in the U.S.A. with their privileged, socially integrated, economically secure position in China. That old age psychoses are infrequent in China is an impression Dunham shares with other authors, and while as yet without statistical proof, it is unlikely to be devoid of some foundation. The many valuable suggestions presented by the survey of Faris and Dunham await further exploration. A comparative survey of the status of the aged in urban and rural communities, for example, might throw more light on the specific social factors favouring the manifestation of old age psychosis in the former, and lead to proposals for an attack on what Lewis has justly called a "major problem in psychiatry."

Recent years have seen an awakening of social responsibility towards the aged and chronic sick which has found some expression in a number of important surveys of their special problems. Among these the reports issued for the Trustees of the Nuffield Foundation (1947 and 1948), and one by a Committee of the British Medical Association (1947), may be mentioned as being the most important. The Rowntree Committee's report published for the Nuffield

Foundation (1947) deals with the incomes and living conditions of the old, the homes and institutions provided for their care, their employment and recreational activities. Commenting unfavourably on the conditions under which the aged live at present in public assistance institutions, they recommend the establishment of small residential homes for 30-35 residents to accommodate all those aged now cared for in institutions, as well as many of the 95 per cent. at present struggling at the cost of great hardship often to their families as well as themselves to maintain their independence. Many of these independent aged would prefer to enter such hostels, having few restrictive rules and a homelike atmosphere. The Committee urge the provision of more clubs and facilities for recreational activity for the aged.

In their reports both the Rowntree Committee and that set up by the B.M.A. make proposals for a better co-ordinated Medical Service for the elderly. It is suggested that the central feature of the Service should be a geriatric unit attached to a general hospital. All cases of disease should be admitted here for thorough investigation, treatment and assessment of their long-term needs. With active treatment many of the old will be able to return to ordinary life, at least for long periods. The reluctance of the old to enter hospital, which all too often in the past meant taking their last leave of home, will be overcome once a two-way traffic between residential home and hospital has been established. The setting up of suitable hostels to accommodate homeless recovered patients and of long-stay annexes for irremediable cases is recommended. Seriously disturbed psychiatric patients should be admitted to an observation ward attached to the geriatric unit and thence, after assessment by a psychiatrist, to a mental hospital, if likely to benefit from active treatment, or a long-term annexe if the condition is one of undisturbed dementia or psychosis.

The second of the surveys published for the Nuffield Foundation (Sheldon, 1948) was based upon a study of a random sample of 477 old people. General health was unexpectedly good in this group, only 29 per cent. being under treatment at the time they were visited. Some two-thirds retained their ability to get about, 2.5 per cent. were bedridden. Limitation of movement was often imposed by fear of traffic due to deafness, vertigo, and a liability to falls. Sheldon considers this last factor worthy of further investigation. In addition to its more obvious causes, he found a sudden loss of muscular tone responsible in many cases. He suggests that this may be due to changes in the central nervous mechanisms subserving posture. Some 11 per cent. of cases were held to have slight mental impairment consisting of apathy, depression, failure of memory, rambling speech, and a tendency to morbid anxiety. Depression was an especially frequent finding in the sample. Some 4 per cent. had severe mental deterioration, while only 0.8 per cent were considered certifiable. (More detailed psychiatric investigation supported by psychometric studies would probably have shown a higher incidence of mental disorder and deterioration.) These old people faced conditions of great hardships with fortitude and resilience, but often, though apparently living alone, they were members of a family group, having children or other relatives who either lived nearby or visited them regularly. This is not to be taken as contradicting the view held

by most observers that the old are no longer permitted an active participation in the life of the family as in former days, and that there has been a serious decline in the responsibility felt and accepted by the young for their aged relatives (Rowntree 1947).

Many other organizations have been active in promoting the welfare of the aged and investigating their special problems, the most notable being the National Old People's Welfare Committee, on which thirty-four voluntary bodies are represented, the Committee, formed by the London Council for Social Service in 1943 and the Club for Research on Ageing. At conferences the latter organized in 1946 and 1948 a number of valuable contributions were made.

These developments are described here as they would appear to be well worth the study of psychiatrists, who in mental hospitals care for a not inconsiderable fraction of the total number of chronic and aged sick. In research on and rehabilitation of the old, the aid of the various bodies to which reference has been made might be enlisted with greater advantage.

Prophylactic measures to ensure that the old should not only remain out of hospital but maintain full health and vigour have also been discussed by a number of individual authors (Bowman, 1945 ; Stieglitz, 1945, 1946 ; Lawton, 1945 ; N. Lewis, 1945 ; Cameron, 1945). The abandonment of compulsory retirement at calendar age is generally urged. It is not only harmful to the old, who thus lose their sense of purpose and sustaining habits, but also wasteful for society, which is deprived of the services of those often old in little beyond years and experience. A socially responsible attitude towards the old should ensure their economic security and change rather than terminate their activities, in accordance with their altered capacities. Educational preparation for ageing should include the encouragement in advance of leisure occupations. Adequate provision ought to be made for social and recreational clubs for the old. It is encouraging to learn that there are now a hundred such clubs in London with a total membership of 10,000 (*Brit. Med. J.*, 1946). Their value was illustrated by the work of Goldschmidt (1946). She studied the effect of four different environments on four separate groups of fifty old people. One of these groups found in a club the opportunities for human contact and self expression so conspicuously lacking in the lives of another group of fifty patients before their admission to a hospital for the old. Of all causal factors examined, she judged this lack of social integration to be the "most powerfully averse to mental health."

Believing that the unhappy plight of the aged is largely the product of modern urban civilization, some authors (Cameron, 1945 ; N. Lewis, 1945) have emphasized that fundamental changes in the social and cultural pattern of society will have to be effected before we can expect any large-scale solution to the problems posed by the growing number of aged.

3. CARE OF THE AGED.

There has been a vigorous movement for the reversal of the attitude of apathetic neglect towards the aged sick that probably owed much to the tradition established under the Guardians of the Poor, who provided the aged in institutions with little beyond custodial care in common with other paupers.

Setting to work in wards where formerly the aged lay in bed year after year without proper examination, let alone treatment, pioneers such as Warren (1946, 1948), Cosin (1947, 1948), Howell (1946) have shown that in suitably planned and cheerful surroundings with active treatment and an imaginatively conceived programme of rehabilitation something like 60 per cent. of aged sick could be returned to their homes or long-stay annexes, and many others prevented from becoming bedridden. One of the highest tributes to their work is that they can claim to have captured the enthusiasm of nursing and auxiliary medical staff for this work. The revolution in the atmosphere of chronic wards achieved by active treatment has been well portrayed in an excellent series of articles in the *Lancet* (1947) on the modern care of the aged.

Some workers (Brooke, 1949) in an attempt to deal with the pressure on chronic beds have established a domiciliary service for the aged, which provides hot meals in their homes and transport to and from hospital for investigation, physiotherapy and other treatment. A team of psychiatrist, social worker and occupational therapist could well play a valuable role in such a service. Domiciliary evaluation, treatment and rehabilitation would attack the case of senile mental disorder at a stage rarely seen in present-day practice, and thus possibly reduce the demand for mental hospital beds. The establishment of advisory centres staffed by doctors qualified to give "child guidance in old age" has been recommended (Goldschmidt, 1946; Mackintosh, 1947). Such centres would be complementary to a domiciliary service.

During the past five years geriatrics has to an increasing extent come to be recognized as a specialized branch of medicine. The establishment of geriatric units has been generally urged in the belief that they would confer a new dignity to the work of caring for the aged (Johnson, 1946; Affleck, 1947).

In the United States great interest in the problems of the aged is reflected in the launching of two journals devoted to problems of old age (*Geriatrics* and *The Journal of Gerontology*). A clinical volume edited by Stieglitz on *Geriatric Medicine* contains a chapter by W. and C. Miles on the psychological changes attendant upon old age, while Overholser contributes a brief article on mental diseases in later life. *The Care of the Aged* (Thewlis, 1946) covers no new ground from the psychiatric point of view. An important symposium edited by Kaplan (*Mental Disorders in Later Life*, 1945) contains articles written by various authors on the social, psychological, physiological as well as psychiatric aspects of old age; reference is made to the separate chapters in the appropriate sections of this review.

Disease processes in old age have their own laws and regularities, hitherto little explored. Contrasting disease in youth and senescence, Stieglitz (1945) emphasizes that in old age causative factors tend to be endogenous, diffuse and cumulative. Time of onset is remote, and the course chronic and progressive. An increased vulnerability to other diseases commonly results. Some observations by Howell (1944) have added to our knowledge of the natural history of disease in senescence. He points out that degeneration, chronic infection and ischaemia predominate in old age in contrast to cancer, hypertension and various dyspepsias in middle age. A clear-cut diagnosis frequently cannot be made as in younger patients, for disease processes elude

precise definition, and even thorough investigation may throw little light on them. In evaluating the prognosis of disease in the old it is important to observe posture and movement, complexion, expression, skin texture, prominence of veins and arteries, colouring of ears, lips and extremities, as well as the discrepancy between real and apparent age. Systolic hypertension he considers to be the rule in healthy old men—a view supported by the careful investigations of Russek *et al.* (1946), who state that the old maxim “100 plus age” might actually be a fair index of systolic blood pressure. Howell describes a fatal syndrome in old age in which a fall of 20–50 mm. in systolic blood pressure is accompanied by mental confusion. In a report on physical signs in the C.N.S. in old age (1949) he has described the frequent occurrence of inactive pupils, absent deep and superficial reflexes, dysmetria, absent vibration sense in the lower limbs, and patchy analgesia without abnormal serology or classifiable neurological disorder. Careful assessment of the physical status of old patients is becoming increasingly important in psychiatry (*vide infra*), and such additions to the clinical phenomenology of old age deserve the attention of psychiatrists.

4. THE SENILE AND ARTERIOSCLEROTIC PSYCHOSES.

(a) *Aetiology and Clinical Aspects.*

In a symposium on “Ageing and Degenerative Diseases” (*Biological Symposia*, 11, 1945) there were a number of important contributions on experimental arteriosclerosis by Hueper, Page and Dragstedt.

An attempt is made by Hueper to integrate the existing clinical, pathological and experimental data about arteriosclerosis occurring or produced “under conditions excluding the senile factor and the senile period of life.” He cites four fundamental types of anoxaemic causative mechanism, each responsible for a different type of vascular damage. Thus atheromatous lesions are found exclusively in colloidal disturbances of the lipoids and carbohydrates of the plasma. Page relates three known factors to the development of arteriosclerosis—hyperlipaemia, mechanical strain, and a factor which leads to precipitation of plasma lipids on arterial tissue. He discusses possible methods of controlling these factors. Hyperlipaemia may be combated by treating the underlying disease (e.g. diabetes, nephrosis) that causes it. Reduction of elevated arterial pressure influences the second factor. As regards the third factor, iodides, thiocyanate and other substances prevent the formation of atheroma in animals, but no definite evidence as to their effectiveness in man exists. Dungal (1936) believes, however, that the extremely low incidence of atherosclerosis and the low weight of the thyroid in Iceland are due to the abundance of iodine in the food, soil and air. Page emphasizes the distinction between loss of elasticity and atherosclerosis. In the cerebral vessels the former is frequently mistaken for the latter, even on the post-mortem table. Increased systolic pressure with no rise in the diastolic is simply the mechanical result of loss of elasticity, and not due to arteriosclerosis; there is no justification for interpreting it as a compensatory process ensuring an adequate blood supply to ischaemic organs (*cf.* Rothschild).

Dragstedt claims that pancreatectomy produces an increased incidence of

arteriosclerosis in the dog, an animal normally resistant to arteriosclerosis. He suggests that a second pancreatic hormone, lipocaic, may be concerned in the prevention of lipid deposits in blood vessels, and that its absence may condition the high incidence of atherosclerosis among diabetics.

An erudite and stimulating review of the aetiology and pathology of arteriosclerosis by Aschoff (1939) covers ground that is by now mostly familiar, but is still well worth reading. He quotes Davidowski for the view that in Russia severe arteriosclerosis is rare—a phenomenon attributed by this author to the liberal consumption of vodka. In contrast, Mohammedans in Arabia, for whom alcohol is proscribed, suffer, according to Aschoff, from a heavy incidence of the disorder. This paper is included in a volume from Germany which has become available since the end of the war (*Ztschr. f. d. ges. Neur.*, 1939, vol. 167). It is a collection of fully documented but at times rambling reviews of the psychiatric, physio-pathological and psychosomatic aspects of old age. A number of the authors seemed to find it necessary to adorn their papers with unctuous, sycophantic and irrelevant eulogies of Adolf Hitler and his regime. Some of these reports will be referred to individually.

All human beings have it in common that they undergo some mental and physical decline as they age in years. Haldane has pointed out (1941) that genetics has achieved its success by limiting its scope so as to exclude the investigation of the reasons for similarities among different members of the same species such as this. However, there are differences in the rate and mode of ageing between individuals about which genetics should have important things to say. The field has obvious difficulties, but these do not justify its having been left virtually unexplored. Frey (1939) has summarized a number of limited investigations on the problem of inheritance of hypertension and arteriosclerosis. He quotes the work of Weitz (1923), who found evidence for the genetic causation of hypertension. Among other investigations he examined forty-five pairs of monovular twins. Similarity of values for the blood pressure was striking in each case, sometimes despite marked environmental differences. The twin investigations of Verschuer (1929) pointed in the same direction. A review of the genetics of old age mental disorder by Bischof (1939) serves to underline our ignorance of the subject. He quotes the work of Meggendorfer and Weinberger (no reference given). Both these authors have produced evidence for the familial incidence of senile psychosis. They concluded from their investigations that neither schizophrenia nor arteriosclerotic psychosis was genetically uniform with this disorder.

In a series of articles on the senile and arteriosclerotic psychoses Rothschild (1945, 1947a, b and c) has restated his belief in the decisive influence exercised by psychological and extracerebral somatic factors in these diseases. He produces further evidence for the inconsistency between the gravity of mental symptoms and the severity of brain damage. The premorbid personality of patients with arteriosclerotic psychosis renders them vulnerable to mental illness. Its commoner features he gives as seclusiveness, emotional instability, aggressiveness, restriction of interests. Good psychological resistance is associated with somatic factors, in particular with the capacity for compensatory cardiac hypertrophy to offset the cerebral damage.

Rothschild has made a positive contribution by pointing out that too narrow a view has been taken in the past of the aetiology of old age psychoses. The discrepancy between pathological and clinical findings, which he emphasizes, is in accordance with the work of Gellerstedt (1933), Aschoff (1938), and more recently of v. Braunmühl (1940) and Strassman and Krush (1947). However, some of his views involve a number of assumptions which are at present hypothetical. With regard to the role of premorbid personality, one gains the impression, reading the relevant case-reports, that as in much psychosomatic literature the "evils" of personalities have tended to live after them, the good having been "oft interred with their bones." The evidence for the role ascribed to compensatory cardiac hypertrophy and for its association with good psychological resistance receives no confirmation from other sources. Bodechtel in 1932 found severe cortical lesions in cases of cardiac disease without serious mental symptoms. In Rothschild's view such patients should have had symptomatic psychoses. More recent investigations by Rosen and Smith (1943) may be mentioned in this connection. They studied twenty-seven cases of severe old age psychosis. Those with cardiac disease were classified in three grades of severity, and compared with sixteen normals as regards venous pressure and arm to carotid circulation time. They concluded that cardiac decompensation plays little part in the psychoses of the senium when advanced heart disease is not present. It will be evident that further investigation is required before a definite answer can be given to the many questions raised by Rothschild's views. Comparative studies of the clinical status, psychological performance and post-mortem pathology of a large material of psychotic and non-psychotic senescents are called for.

If a poorly integrated personality predisposes, as Rothschild suggests, to arteriosclerotic psychosis a chronic paranoid state ought, on the other hand, according to work done by Alpert *et al.* (1947), to protect against it by preserving the cerebral vessels. In fifty patients, average age sixty-one years, with long-standing paranoid psychoses studied by the latter, a confident diagnosis of cerebral arteriosclerosis could be made only in four cases. This diagnosis was established on the basis of examination of peripheral and retinal vessels, blood pressure, presence of subjective symptoms commonly associated with cerebro-vascular disease, as well as the incidence of psychological features, such as emotional lability, patchy amnesia, confusion and other intellectual defects. They put forward a psychosomatic explanation of the low incidence of disease of the cerebral blood vessels in this group. The paranoid patient, they say, is better able to abreact his emotional tensions in his psychosis than the average person whose hostilities are repressed. Frequent episodes of excitement associated with raised blood pressure also enable him to compensate more adequately for cerebral ischaemia. It is to be doubted, however, whether all cases with cerebral arteriosclerosis were in fact identified by the methods described. Nor is it clear, moreover, why the paranoid psychotic should be in a better position psychosomatically than other psychotics; the claim that he is would appear to be in conflict with the author's statement that he is subject to paroxysmal bouts of hypertension.

The psychosomatic aspects of circulatory disturbances and their psychological treatment are discussed by Schultz (1939). He brings out the reciprocal relationship between affective and circulatory disturbance, but doubts whether any case of hypertension can ever be completely accounted for by psychological factors.

Ten cases were selected by Gold (1943) from a group of three hundred individuals with hypertension to study psychological factors operative in this disorder. Organic causes for their raised blood pressure were held to have been excluded in this small number of cases. A variety of psychopathological characteristics was brought to light, including over-strong parental attachment, energy and over-conscientiousness, as well as inadequate drive, lability of mood, sexual mal-adjustment, paranoid features, etc. The evidence for their causal relationship to the hypertension fails to carry conviction.

Allen (1944) quotes three case-histories to demonstrate that mental diseases in old age are often continuations or recurrences of disorders commencing earlier in life; they also occur in previously unstable personalities that escaped stress before. He admits that such "functional personality disorders tend to become chronic," but points to the frequency of remissions during which the patient may live at home. In another paper (1947) Allen states that a poor prognosis is often given to depressive stupors in old age when mask-like facies and a loss of sphincter control are present. In effect such features do not necessarily signify an organic process, and the condition may prove benign and reversible in spite of them.

Articles on the symptomatology of senile and arteriosclerotic psychoses by Alpers (1943) and Rothschild (1947) cover no new ground. That by the latter contains a very full discussion of the differential diagnosis.

It has long been appreciated that in all mental diseases with an acute onset or florid picture seen in old age, malnutrition is often a contributory cause. Wexberg (1945) has found that acute delirious states occurring in old patients are frequently helped by vitamin therapy, but admits that the evidence that vitamin deficiency is wholly responsible is slender. Both Wexberg and Robinson (1945) think that these conditions are often wrongly attributed to senile or arteriosclerotic processes simply because of the patient's age. Robinson gives the "toxic delirious reactions of old age" a separate nosological status. He describes the clinical picture in detail; diurnal drowsiness, nocturnal restlessness, hallucinations, clouding of consciousness with disorientation and dream-like experiences are common. The patients are noisy, over-active, terrified. There is a history of undernutrition. Urinary incontinence is usual. Mild fever is commonly seen, and loss of weight, exhaustion and dehydration are characteristic. The serum non-protein nitrogen is high, and sugar and albumin are nearly always present in the urine.

Robinson goes too far in the opposite direction in affirming that this condition, because acute in onset and recoverable, cannot be a manifestation of senile or arteriosclerotic psychosis. Few will agree with his statements that acute exacerbations do not occur in the former, or that the latter must not be diagnosed unless there is evidence of a prior vascular occlusion. It is Robinson's belief that all delirious reactions, including delirium tremens, have a

similar pathology, independent of their precipitating cause—an old view still awaiting proof. He has, however, performed a service in emphasizing the frequently benign and transient character of delirious states in old age, and his claim for the specific therapeutic effect of infusions of 10 per cent. glucose in plain water deserves further investigation.

The view expressed by both Robinson and Wexberg that vitamin deficiency plays only an incidental role in the causation of delirious states in the aged deserves further consideration. After the first accounts from Sydenstricker's clinic (1939) of the dramatically successful treatment of stuporose and delirious states in elderly arteriosclerotics with nicotinic acid, it was hoped that many of the acute psychotic states in old age would respond similarly. In fact, apart from the cases developing under conditions of severe deprivation and hardship in prisoners of war or native populations in the east (Spillane, 1947; de Wardener, 1947) and a relatively small number of cases associated with serious physical illness (Slater, 1942; Gottlieb, 1944; Hardwick, 1946; Avery Jones, 1947) and exceptional stress (Roth, 1949), there have been only isolated accounts of psychosis in old and middle age due to vitamin deficiency (Meyersburg, 1945). Unless deficiencies due to unidentified vitamins are at work, or the condition tends to come under observation at an advanced irreversible stage, it would appear that vitamin lack can only rarely by itself cause an acute delirium in old age. It may on the other hand play its part as Robinson suggests as one of a constellation of metabolic factors.

The cerebral form of thrombo-angiitis obliterans has been dealt with in a number of interesting reports. The condition appears to be rare. Scheinker (1944) mentions that in the period 1937-44 he saw only three cases of cerebral thrombo-angiitis obliterans in a department of neuropathology attached to a general hospital, while Perk (1947) quotes Hausner and Allen (1938), who found a 2.2 per cent. incidence of the disorder in a group of five hundred cases of Buerger's disease of the extremities studied at the Mayo Clinic. Reviewing the literature Perk (1947) gives the commoner clinical features as muscular spasms ranging from tics to epileptiform fits, partial or complete hemiparesis, hemianopia, fleeting sensory disturbances, aphasia, apraxia, impairment of memory and clouding or interruption of consciousness. Mental symptoms are infrequent, but range from transient confusional excitement to sustained psychotic disorders. He describes a personal case of a man aged 29 who was observed during 16½ months, in the course of which he had accumulated a variety of diagnostic labels. The psychosis was the first manifestation of Buerger's disease. It consisted of a state of acute manic excitement interrupted by brief periods of coma which were attributed to exhaustion. There were periodic epileptic fits, and as the disease progressed increasingly prolonged episodes of clouded consciousness with perplexity, impulsive destructiveness and auditory hallucinations; in the later stages depressive bouts alternated with manic excitement. Dry gangrene was first noticed after the psychosis had been in progress for some weeks, and continued to advance until, at the time of the patient's removal from hospital after sixteen months, eight of his toes had sloughed off. In a relatively large material of twenty-two cases of the cerebral form of Buerger's disease studied by Lindenberg (1939) the age of

onset of the disorder ranged between thirty and eighty, half of the cases commencing after the age of fifty. This contradicts the common belief that the condition is one of early adult life. In seeking an explanation for the combination in the clinical picture of paroxysmal symptoms with sustained and progressive mental disorder, Perk (1947) points out that two distinct physiopathological mechanisms may be discerned in the condition—a spasmodic disturbance induced by changes in the vessel wall and leading, in the case of the lower limbs, to intermittent claudication, and a progressive occlusion of affected vessels resulting in gangrene. The hypothesis that the neuropsychiatric picture in the cerebral form of the disease is due to these two types of change seems convincing.

A revival of interest in the cerebral complications of rheumatic fever may be partly attributed to the endeavours of Bruetsch. It will be remembered that in an account of autopsy studies in dementia praecox in 1938 this author reported a 9 per cent. incidence of chronic rheumatic infection involving the brain as well as the heart valves. The cerebral changes consisted of a recurrent obliterating endarteritis affecting mainly the meningeal and cortical vessels. He emphasized that the condition is not usually acute, its evolution extending over a number of years. In a study of twenty-eight cases of rheumatic brain disease Bruetsch (1947) has now found a raised sedimentation rate in 87 per cent., while an increased leucocyte count occurred in only 30 per cent. The pathological findings in four new cases are described in this paper. In addition to changes in the heart, rheumatic lesions were found in the vascular system of brain, spleen, kidneys, etc. It must be observed, however, that endarteritis obliterans was not found by van der Horst (1947) in his cases of rheumatic brain disease. The cerebral changes were described by him as those of a meningo-encephalitis. He agrees with Bruetsch, however, that psychosis due to rheumatism may not begin until years after the appearance of polyarthritis.

Our knowledge of the fate of intelligence in the course of ageing of mental defectives is still in its infancy. Kaplan (1945) has summarized the available facts in this difficult field. In an investigation of mental decline which he carried out in sixty-six morons whose average age was forty-one, the Stanford-Binet test was performed on two occasions in each patient after an average interval of about 15 years. The decline was negligible, amounting to 6.6 mental-age months. More surprisingly, nine patients showed a gain in mental age. Vocabulary remained remarkably constant, in males it had even improved. Examining the results of other workers, Kaplan concluded that tests requiring speed and abstract thought would probably have shown more pronounced deterioration. In addition to early deterioration, the absence of the stabilizing and protecting influence of family life in many defectives puts them at a much greater disadvantage in old age than individuals of normal intelligence. However, most defectives never manifest psychoses, although some in the higher I.Q. grades survive to develop senile or arteriosclerotic psychosis. According to Kaplan schizophrenic and affective psychoses are rare below the moron level, if they occur at all; in higher grades symptoms usually develop in the latter half of life. Many transient and acute mental disturbances in defectives cannot be easily classified in the conventional diagnostic categories.

In a study of the life duration of low-grade defectives in an institution, Kaplan found the average life span of 424 imbeciles to be twenty-seven years and of 344 idiots nineteen years. However, 16 per cent. of imbeciles and 7 per cent idiots survived beyond fifty years.

The premature onset of senile dementia in mongoloid idiots is common according to Kaplan, and Jervis (1948) has reported three fully studied examples of the phenomenon. At the ages of forty-seven, forty-two and thirty-seven respectively, personality changes and mental deterioration (assessed at twenty to thirty points of I.Q.) were observed in each case. Owing to limited intelligence the mental symptomatology was scanty, but apathy and sullenness, deterioration of habits and episodes of excitement, evidently in response to hallucinatory experiences, were noted. The abnormal physical signs were fine tremors of the hands, increased deep reflexes, and in one case paresis of the extremities. Pathologically, evidence of senile changes was obtained consisting of degeneration of neurones, senile plaques and neurofibrillary changes. As three out of five cases of mongolism studied showed the pathological senility described, Jervis suggests that the factors which play a role in mongolism may be similar to those operating in senile dementia, and that the endocrine deficiencies to which the former has been attributed may be common to both. All that would appear to be warranted is that mongolism predisposes to precocious ageing, as it does to many other pathological processes.

Crime in old age has been discussed by East (1944). He shows that the decrease in incidence of indictable crime in the period 1911-28 as judged by the number of convictions was greater in men over sixty than that in any other age group. There was a further reduction of crime rates in the elderly between 1929-38. The relative frequency of acquisitive, sexual and aggressive crimes was the same above as below sixty. Bigamy was rare as compared with homosexuality, while indecent exposure, paedophilia and the sending of obscene letters through the post comprised 60 per cent. of the total offences among psychotics of the group. In the aggressive group attempted suicide was the most common offence after sixty. It would have been interesting in this connection to learn the number of these in which the aid or advice of a psychiatrist had been sought by the court. Homicidal crimes were fourteen times more frequent in the under sixties than in the over sixties. Simple senile dementia was commonly associated with crime of a minor character, depressive, manic and paranoid syndromes with serious crimes.

In America in 1940 the number of prisoners above sixty-five was about one-twentieth of that between thirty-five and forty-four in both sexes. A high proportion were first offenders. There was a higher incidence of suicide in men than in women. It was especially common among Chinese and Japanese, but infrequent among Negroes and Indians (Jones and Kaplan, 1945).

(b) *Laboratory and P.M. Findings.*

The C.S.F. in sixty-five cases of arteriosclerotic and senile psychosis has been studied by Riebeling (1939). In arteriosclerosis he found many more cases of increased protein than in seniles and preseniles. In two-thirds of cases with a previous apoplexy there was a positive finding. Increased protein in

these cases could not be accounted for in his view by haemorrhage into the subarachnoid space. In simple senile dementia the protein tended to be low, otherwise the findings were negative. In presenile dementia there was often an increase in protein.

As opposed to these findings Blalock (1944) concluded from a study of 369 cases that spinal-fluid protein and sugar content in arteriosclerotic psychosis as well as senile dementia are within normal limits, and that the findings cannot be used in differential diagnosis between the disorders. It is to be doubted whether the calculation of average figures for such a large number of cases, all presumably at different stages of development, is the best way of discovering further differential diagnostic criteria for these conditions. Study of selected groups of cases might have yielded more positive results.

Following up suggestions from Quastel's work in catatonics Stern *et al.* (1945) studied hippuric acid synthesis during psychoses of the involutional and old-age group. They found faulty detoxication three times more common in psychotics over sixty than in mentally normal people of the same age group studied previously. Cases of senile dementia gave lower figures than affective or arteriosclerotic disorders. Comparison of the cases among themselves showed that gross differences in diet, body weight, blood pressure and urinary excretion could be eliminated as causes of error. The significance of the findings is not discussed.

Strauss and Greenstein (1948) studied the E.E.G. in ninety-five cases of cerebro-vascular accident. A correlation was observed between the state of consciousness and the type of E.E.G. abnormality. However, gross hemispheric lesions were not always associated with E.E.G. change, although when a focus was located it corresponded to the site of the lesion as judged from clinical findings. Of fourteen cases with convulsive seizures not one showed epileptic features. Discussing the diagnostic value of their findings the authors suggest that asymmetrical delta activity or a definite focus favours a diagnosis of cerebral tumour as against cerebro-vascular disease, while a diminution of the degree of abnormality in successive records is in favour of the latter.

In a clinical and electro-encephalographic investigation of fifty-three arteriosclerotic and senile patients, Liberson and Sequin (1943) found that the markedly abnormal records with slow activity were mostly seen in patients with a combination of confusion and irritability. One-third of the records fell into this category. Patients with the complex of anxiety, agitation and delusions, on the other hand, tended to have normal or borderline records. This group of cases, the authors suggest, may therefore be related to involutional melancholia.

The cold pressor reaction was studied in twenty cases of cerebral arteriosclerosis and fifteen of meningo-vascular syphilis by Becker *et al.* (1948). Increased vasopressor activity was demonstrated in both groups of patients, and was most marked in cerebral arteriosclerosis. The controls used in the experiments do not seem to have been judiciously selected.

Strassmann and Krush (1947) studied the pathological findings at post-mortem in fifty old patients: twenty were senile psychotics, twenty-five had cerebral arteriosclerosis, one was an alcoholic; the remainder were paranoid

schizophrenics. The commonest cause of death was bronchitis and bronchopneumonia; others were pulmonary embolism, carcinoma and tuberculosis. The leptomeninges were thickened in all cases, cerebrospinal fluid increased and the basilar arteries sclerotic. Increased deposits of iron were frequent in the extra-pyramidal system, around and in the walls of capillaries and arterioles, particularly in the globus pallidus. Many senile plaques were present in the cortex and occasionally in basal ganglia and cerebellum in 66 per cent. of the cases. In the remainder, few or no senile plaques were present. Nevertheless, 12 per cent. of this group had in fact been given a diagnosis of senile dementia. Ischaemic softening was present in 68 per cent. The results underline once again the partial truth that a diagnosis of senile or arteriosclerotic psychosis is, referring as it does, and often inaccurately, to the preponderance rather than the exclusive presence of one or other type of pathological change.

Binswanger's disease (chronic progressive subcortical encephalopathy) is generally attributed to sclerosis of the long medullary vessels supplying the white matter of the cerebral hemispheres. Neumann (1947) has reported the case of a woman of sixty-two who was admitted to hospital with a predominantly depressive picture. During fifteen years of hospitalization there were periodic convulsions, increasing left hemiparesis and dysarthria. At autopsy there was almost total subcortical demyelination on the right side, changes on the left side being of a more patchy character. The similarity of the observed changes to those found in Schilder's disease was noted. Neumann suggests that occurrence of cerebral arteriosclerosis in these cases may in fact be fortuitous.

A condition studied in three juvenile patients by Waggoner and Malamud (1944) is thought by them to constitute a new syndrome. It was characterized by catatonic-like states of excitement or stupor, followed by complex neurological and vasomotor disturbances which terminated fatally. They compare it with similar manifestations occurring as a complication in the course of schizophrenic psychoses and psychoneuroses. The pathological findings were non-inflammatory irritation of leptomeninges and choroid plexus, widespread foci of ischaemia in the grey matter, and perivascular areas of demyelination in the white substance. These changes were held to be of circulatory origin, although the blood vessels were normal. The authors attributed the syndrome to the effects of psychic stress in patients with a "vulnerable vasomotor system."

(c) *Psychometric Studies.*

Of all the people who have attempted to depict senescence, psychologists have perhaps been the most successful in defining some of its most characteristic features in terms of objective, quantitative variables. Bartlett (1946) has pointed out that ageing may be compared in its effects on psychological performance with extremes such as heat, humidity and noise. Each produced an increased liability to fatigue susceptible of measurement in different ways.

Some of the special difficulties of testing the old have been emphasized by Jones and Kaplan (1945). Motivation does not remain static throughout life, and it is pertinent to remember that it is ability and not capacity that is

measured by a test. Inferiority feelings often hamper the old, and time limits place them at a further disadvantage. They are at their best in tasks for which they can utilize their larger fund of experience, whereas in novel situations they are relatively inefficient.

The findings of most authors are in accordance with this last generalization. Investigating twenty senile patients Halstead (1943) found a striking impairment in those tests calling for ingenuity, in contrast to the preservation of rote memory, vocabulary and arithmetic. He believes that tests for senility should be short, as straying attention, difficulty in comprehension and perseveration tend to distort the results.

The structure and organization of intellectual abilities in old age was studied by Margaret Eysenck (1945a). She gave a battery of psychological tests individually to eighty-four cases of senile dementia, repeating them after four months. She concluded that the organization of mental ability in old age was profoundly altered as a result of the severe deterioration of abstract reasoning ability, as compared with the slight impairment of abilities involving the reactivation of past knowledge. She considered that her results were best accounted for in terms of Cattell's hypothesis that there are two types of adult mental capacity, the "fluid" and the "crystalline," the former based upon ability to perceive new relations, and the latter upon long-established habits in a particular field which no longer require "insightful perception for their successful operation." The former declines, while the latter remains comparatively stable and determines achievement in later life. A factorial analysis revealed a general factor accounting for 43 per cent. of the variability and three group factors concerned with speed, memory, and physical strength and dexterity. In another series of experiments she used the matrix form board in one hundred cases of senile dementia (1945). There was considerable quantitative deterioration, but types of error made, the reasons for these errors and the order of difficulty of the problems were essentially the same for seniles as for 104 children and 2,790 adults with whom they were compared. She concluded from her results that the ability tested in normals and seniles was qualitatively identical. It detracts from the value of these important investigations that no attempt seems to have been made to eliminate cases with focal organic lesions, such as apraxia, aphasia and agnosia, nor clinical entities, such as the presenile dementias, nor arteriosclerotic psychoses, all of which may have confused the issues under examination by rendering the material heterogeneous. It is also to be doubted whether achievement in the tests described offers an adequate incentive to senile patients.

Foulds and Raven (1948) conclude, from the rate of decline of abstract thought after twenty-five, that at eighty the average person's capacity to perceive new relations is no greater than that of a child of eight. Ability to recall information, while usually remaining constant from thirty to fifty-five, continued to increase, in individuals of above average ability, until sixty. Their findings were in accord with the view that vocabulary level was a reliable index of best intellectual level hitherto attained.

This view, generally accepted among psychologists, is contested by Ackelsberg (1944). She gave a battery of vocabulary tests to fifty cases of simple

senile dementia, who were graded on a three-point scale for degree of deterioration. She found that the latter was accurately reflected by performance in the tests. Without further information as to the criteria by which degree of deterioration was assessed before testing it is difficult to evaluate these results. Madonick and Solomon (1947) tested fifty men and women between sixty and eighty-five with the Wechsler-Bellevue Scale. I.Q.s. ranged between 85 and 140, and verbal and performance tests held up equally well. However, the group was unrepresentative, consisting of formerly successful professional and business men who had got into financial straits.

Comparatively little is known of intellectual status in the different clinical syndromes of old age as reflected by performance in objective tests. A small but interesting investigation was carried out by Meyrat (1945) in senile and presenile dementia with tests for verbal, practical, visual, tactile and stereognostic memory. Memory functions showed involvement or preservation independently of each other. Whereas ability to recall a stimulus had disappeared within three seconds in cases of Alzheimer's disease, in senile dementia the interval was usually two to three minutes. There was a certain but incomplete parallelism between impairment of memory and of the function involved in the registration or execution of the memorized material, i.e. praxis, speech, writing, etc. Memory for recent events was not always more affected than remote memory.

Studies with projection tests have been few in this field. Hitch (1943) examined a case of cerebral arteriosclerosis with the Rorschach test, and insists that he was able to make the diagnosis independently of any clinical information about the patient. Prados and Fried (1947) investigated personality structure in older age groups with the Rorschach method. They found impoverishment of creative intellectual faculties, evidence for diminished control of instinctive demands, and a tendency to reaction with anxiety.

(d) *Psychopathology and Psychotherapy.*

Psychopathological and therapeutic aspects of psychiatric disorders in old age have been discussed by Rockwell (1945), Cameron (1945), as well as by Gitelson (1948) and Mittleman (1945). Rockwell says that insecurity and the lower threshold of anxiety undermines confidence and evokes protective attitudes, such as tenacity and over-cautiousness. The hypochondriacal concern with bodily functions is likewise reactive to impairment of physical security. Panic reactions evoked by stirred-up sexual desires and fixed attitudes of resentment and "aversion" figure prominently in the clinical picture. Neurotic illness often overwhelms the patient in old age, and orthodox psychoanalysis is fraught with danger. A distributive analysis is the treatment of choice, its direction dictated by the patient's immediate needs and current attitudes. The approach should be constructive throughout, the psychiatrist taking full responsibility for planning the patient's activities, which should include suitable occupation and recreation.

In an interesting essay on neurosis in the aged, Cameron (1945) points out that the very qualities which enabled them to succeed in earlier life may hinder their adjustment to a passive and subordinate role in old age. Having lost

much of their elasticity, they are yet asked to make the most difficult adjustments. Their sustaining habits gone, old conflicts, formerly submerged by absorbing activities, now reappear in an unresolved form. Fatigue and hypochondriacal pain are used with neurotic aggression to evoke sympathy.

Some of these articles contain much psychological common sense. However, when clinical syndromes in the old are described, the dominant features of which are anxiety, aversion, hypochondriasis (Rockwell), and even compulsive symptoms (Cameron), it is surprising that no mention is made of the existence of endogenous affective disorders in the aged, in which these symptoms are notoriously prominent, often to the exclusion of overt depression. As conditions arising *de novo*, or afresh after remission, these disorders of predominantly constitutional origin must surely be more common in old age than neuroses, yet even the problem of differentiating them is not considered. The omission is a serious one, for the affective psychoses of old age often respond dramatically to physical treatments (*vide infra*).

(e) *Prognosis.*

A change in the habitual surroundings of mentally sick old people is well known to be followed often by a deterioration in their condition. The fate of old age psychotics after admission to hospital is therefore a problem of some importance. It has been strikingly portrayed in a number of follow-up studies. Beckenstein and Gold (1945) studied two groups, each of one hundred consecutive patients, one with senile and the other with arteriosclerotic psychosis. They had been admitted in a three-month period three years previously. The study showed that the total duration of the illness in senile psychosis tended to be one to three years; in cerebral arteriosclerosis it was less than two years in 70 per cent. of cases. The latter illness carried a better prognosis for survival. 76 per cent. of patients with arteriosclerotic psychosis who left hospital did so within two months of admission, the remainder within a year. No less than eighty-seven of the patients with senile psychosis had died after three years, 63 per cent. of them within three months of admission, and 47 per cent. within one month. Sixty-one cases of cerebral arteriosclerosis were dead within three years, 69 per cent. of these within three months of admission, and 46 per cent. within one month.

Camargo and Preston (1945) studied 683 patients over sixty-five admitted to a mental hospital for the first time; 85 per cent. of these were cases of arteriosclerotic or senile psychosis. A follow-up showed that 47 per cent. of the latter group died in the first year and 8 per cent. were discharged. During the second year 11 per cent. more died and only 1 per cent. were discharged. 66 per cent. had died after three years, 10 per cent. had left, and 24 per cent. were still in hospital. It would seem, therefore, that well over one-half the cases of old age psychosis admitted to hospital die or are discharged within the first year after admission. After three years the great majority are dead or out of hospital.

A report by Pollak (1945) compiled from the records of two thousand patients who came to autopsy in a twenty-year period conflicts with these figures. One quarter of the cases were diagnosed as psychosis with cerebral

arteriosclerosis. However, only in one-quarter of these was death attributable to arteriosclerosis (cerebral haemorrhage, coronary thrombosis, etc.); some 50 per cent. succumbed from pulmonary disease. The mean age at death of the cases of arteriosclerotic psychosis was seventy-one, and this age was exceeded in more than one-half the cases. Now a substantial proportion of patients with this disorder first manifest symptoms in the sixth or early part of the seventh decade. Moreover, in the survey carried out by Beckenstein and Gold over two-thirds had been ill for less than six months on entering hospital. If it is correct that most cases are dead within two to three years (*vide supra*) the ripe old age attained by Pollak's cases is rather remarkable.

A rather more optimistic note than that in the first two reviews was struck by Palmer *et al.* (1943), who found in their cases of old age psychic disorder a social recovery rate of 25 per cent. Cases complicated by physical factors had a better prognosis. They believe the recovery rate can be doubled by active and energetic treatment.

(f) *Physical Treatment in Old Age Psychoses.*

The diagnosis of depression and schizophrenia in old age is complicated by the fact that the clinical picture is usually complicated by organic features owing to the presence of senile, arteriosclerotic or both types of pathological change in the brain. There are also difficulties of a more subtle character. In the first place the interaction of a depressive illness and the effects of arteriosclerotic brain damage tends to create complex syndromes, which cannot be accounted for by a simple process of addition of the symptoms contributed by each process. Moreover, a genetically determined process, such as schizophrenia or manic-depressive psychosis, may be expected to show phenotypic variations according to the age at which it is manifested, for both the degree of integration of the prepsychotic personality and the physiological environment will make some contribution to the total picture of the illness. Thus, as is well known, the proportion of schizophrenics showing predominantly paranoid features increases with age, although a large percentage of paranoid psychoses are genetically uniform with the catatonic and hebephrenic varieties of schizophrenia. Apathy is perhaps one such character conferred by senescence on a depressive illness; it may give a misleading impression of dementia.

The difficulties in diagnosis naturally increase the later in life a psychosis appears, and there is evidence to suggest that in depressions they are for this reason more likely to be encountered with males. For Penrose (1942) has shown that the age of onset of depressive illness is significantly higher in men than women owing to a differential effect of selection on a deleterious dominant gene in the two sexes.

It is such difficulties in the way of disentangling the effects of a reversible psychosis from the various changes attendant upon old age that have in the past led to the attribution of too hopeless a prognosis to psychoses in the old. Since the advent of physical methods of treatment, however, experience has led to a more sanguine attitude; there has been an increasing tendency in recent years to employ these methods. One result often recorded following such

treatment has been the disappearance of features that would be commonly attributed to the irreversible degenerations of old age (Mayer-Gross, 1945).

Evans (1943) treated fifty consecutive patients over fifty with E.C.T. and metrazol. Seventeen were over sixty and five over seventy. Forty recovered or improved sufficiently to be discharged home; only ten were unimproved. An interesting case was one with depression complicating myxoedema. Only when E.C.T. was given did the depression disappear. In a series of seventy-six patients over sixty treated by Mayer-Gross (1945) thirteen patients made a complete recovery and only fifteen failed to show any improvement. Three out of the six cases of senile and arteriosclerotic dementia recovered or improved. Twenty-one patients were discharged from hospital. In only one of the six deaths was the cause possibly connected with the treatment. Twenty-eight of thirty patients over seventy treated by Wilbur and Fortes (1947) showed improvement after a course of E.C.T. Follow-up studies showed that half of their patients were sustained social recoveries. Prompt treatment of recurrences nearly always produced early remission and prevented prolonged hospitalization. Patients over eighty have been successfully treated by Feldman *et al.* (1946).

E.C.T. has also been used in old people in the presence of physical conditions formerly thought to contra-indicate it. Heart disease, hypertension and arteriosclerosis (Napier, 1944; Gallinek, 1947, 1948) have been shown in this way not to be obstacles to successful treatment. The precise indications for curare in old age remain to be worked out. There is no definite evidence that it diminishes the risk where no definite physical disease is present, but exceptional frailty, severe hypertension and previous fractures are generally accepted as indications for its use. The technique of curare-modified E.C.T. has been described in detail by Hobson and Prescott (1947) and Shepherd and Watt (1949). Inanition is common in old age psychoses, and the increased metabolic demands made by physical exertion during E.C.T. may occasionally precipitate an acute vitamin deficiency. Severe and sustained confusional states may develop in this way with the clinical picture of pellagra or Wernicke's encephalopathy (Roth, 1949). Modified insulin to stimulate appetite and vitamins to make up for latent deficiencies are, therefore, essential preliminaries to treatment with E.C.T. where the history suggests that diet has been inadequate.

The result of prefrontal leucotomy in four women over sixty with depression has been described by Myerson and Myerson (1947). In three cases E.C.T. had been given previously with partial recovery which was not permanent. The operation brought relief from tension in each case, the patients leaving hospital to meet increased responsibilities with greater success than before operation. Chronic fatigue in one patient remained. The authors strongly recommend leucotomy in otherwise intractable psychoses of old age.

Aminophylline was given by Reese and Kant (1947) to disturbed patients with cerebral arteriosclerosis and hypertensive encephalopathy in an attempt to improve the cerebral circulation by vasodilatation. Twenty-three out of thirty-two cases improved, including all cases with confusion and clouding of consciousness. Memory and retention defect were most resistive to treatment.

Physical symptoms were alleviated, and there were no fatalities. The effect of aminophylline on the cerebral circulation is not known; the suggestion that it acts as a dilator of cerebral vessels, offered by this piece of work, requires further confirmation. Treatment of twenty patients between sixty-eight and eighty-eight with vitamin B complex for two months was carried out by Wadsworth *et al.* (1948). Some clinical improvement was recorded, but no significant change in performance in psychological tests. Vernon and McKinlay (1946) tried the effect of methyltestosterone on the psychological performance of senile patients. Changes produced were small, inconsistent and often negative.

The facts suggest that arteriosclerotic and senile damage is not necessarily relevant to the psychoses developing in old age, nor always a hindrance to some degree of recovery in response to physical treatment. In the case of shock treatments this involves risks, but these must always be balanced against the dangers to life from suicide and inanition and the hopeless misery endured by the patient. The time has come for the use of E.C.T. and other physical treatments as a diagnostic test in the psychoses of old age to differentiate those which respond from those which resist treatment. The basis may thus be laid for the creation of a more soundly constructed nosological subdivision of mental disorder in old age than exists at present. The tendency has been in the past to relate the total picture of the senile psychoses, including its clearly depressive components, to the pathological changes found at post-mortem. It is at least possible that the depression, in so far as it is separable from the more purely cognitive and intellectual defects, has no more of a neuropathological correlate than has been discovered for it so far in earlier life. Some of the inconsistencies noted by Rothschild (*vide supra*) may have arisen in this way. Follow-up and post-mortem studies of cases responsive and resistant to physical treatment may throw more light on the difficult aetiological problems in this field.

5. PRESENILE PSYCHOSES.

(a) *General Theory.*

The aetiology of the presenile psychoses and their relationship to the ageing process in the nervous system have once again been the subject of discussion.

Newton (1948) has dealt with the nosological status of Alzheimer's disease. He bases his conclusions on a study of the brains from 150 consecutive autopsies at a mental hospital. His pathological findings are of considerable interest. Senile plaques and neurofibrillary changes were found—in thirty-two out of seventy-six cases of affective psychosis, two of seventeen cases of schizophrenia (the smaller proportion is explained by younger age at death), four of seven paranoid psychotics, and fifteen of twenty-three cases of organic dementia. No plaques or neurofibrillary changes were observed in any group below the age of fifty, but in the age group fifty to sixty-four 11 per cent. of males and 29 per cent. females showed plaques, while the corresponding figures for the age group sixty-five to ninety-six were 54 per cent. and 77 per cent. Since the quantitative severity as well as the incidence of the pathological changes seemed to be a function of age, Newton concluded that no clear

distinction could be made between "normal" senility, senile dementia and Alzheimer's disease. He suggests that the three phenomena should be classified in a single category called "Alzheimer's dementia," since they were "three different names for the same process."

That the quantitative pathological differences between the three conditions are not reliable guides in diagnosis without clinical data is generally agreed. However, where the distinction is between a rare and rapidly fatal dementia with focal symptoms of a rather characteristic kind on the one hand, and relatively benign and slowly progressive disorders on the other, a diagnosis is undoubtedly of practical value even if it cannot always be made with confidence, and whether or not the processes can be clearly distinguished from each other by present-day pathological methods.

Newton observed in his material that histological changes occurred in the brain at an earlier age in females than in males. This is in accord with the well known preponderance of women over men in Alzheimer's disease. He suggests a possible genetic explanation of these facts, along the lines of that put forward by Penrose for the difference between males and females in the age of onset of depressive illness (*vide supra*). As in the latter disorder, postponement of the age of onset of Alzheimer's disease would be greater in males owing to their longer reproductive life, so that the condition would appear at an earlier age in females. Why it should therefore be less common in the male sex is not clear from Newton's account, but can be understood if it is assumed that manifestation later in life would make it a less acute disorder and more difficult to differentiate from senile dementia. It would then tend to be identified more often in females. This is an attractive hypothesis which deserves further investigation, but in its present form probably over-simplifies matters. Although several examples of dominant inheritance in Alzheimer's disease are on record and another family has been described recently (Essen-Möller, 1946), genetic transmission has been only infrequently reported as compared, for instance, with Pick's disease. Detailed investigation might, of course, have revealed a genetic cause in a much larger proportion of cases, but it cannot be assumed meanwhile that a dominant gene is the only cause of the disorder. The occurrence of the disease among the progeny of a first-cousin marriage, for example (Löwenberg and Waggoner, 1934), suggests that a recessive form may exist. This type of inheritance would be incompatible with the hypothesis under consideration.

Newton's belief that senile dementia and Alzheimer's disease are a single entity would demand that they should be genetically uniform. Evidence for this is at present very slender. A few dubious pedigrees have been published pointing in this direction (Löwenberg, 1937, etc.), but it must be remembered that senile dementia is exceedingly common, whereas Alzheimer's disease is rare. (This is itself difficult to explain if they have the same genetic cause.) Their co-existence in isolated families might, therefore, be expected to occur by chance.

Jervis (1945) believes that the basic process common to all the presenile dementias is atrophy of nerve cells and fibres with a secondary reaction of glia. The more conspicuous abnormalities such as senile plaques seen in Alzheimer's

disease he would explain as possibly due to certain contingent factors superimposed upon the fundamental pathological process of atrophy. Stern and Reed (1945) drew a similar conclusion from a study of two cases dying after a rapidly progressive dementia, and suggested that the changes superimposed upon the primary ageing process may be reversible. Presenile dementias, according to Jervis, are the expression of "limited viability and premature ageing of the brain or certain parts of it." Quoting Raymond Pearl's evidence for the hereditary determination of the duration of life and its possible modification by environmental factors within limits, he expresses the view that the impact of contingent exogenous factors upon the genetically determined process of ageing may render it premature so as to cause diseases such as the presenile dementias. This theory could be used to explain why senile dementia is common, while presenile psychoses are rare even if Alzheimer's disease and senile dementia are fundamentally identical processes as Newton suggests. However, it would be difficult to reconcile such an explanation with genetic transmission of the presenile psychoses without the aid of further complicated hypotheses.

The suggested unity of presenile and senile psychoses is really an extension of Gowers' concept of "abiotrophy," which attributed the heredo-degenerative disorders to precocious ageing of the C.N.S. Some evidence validating this concept has recently appeared. Meyer and Nevin (1948) have drawn attention in an important communication to the similarities between the changes in the C.N.S. in old age and those seen in the systemic degenerations. It has been suggested (Roth, 1948) that the recently demonstrated genetic heterogeneity of many of the degenerative disorders opens the possibility that such similarities may have a genetic basis.

Uniovular twins discordant for Pick's disease have been described by Becker (1948). The surviving member of the twin pair remained symptomless fourteen years after the disease commenced in the affected one and for seven years after her death. Uniovularity was convincingly established. The author gives an explanation for the discordance in terms of a rather diffusely expounded theory of "developmental lability," which seems to the reviewer just a restatement of the fact that the twins were dissimilar. He reviews the literature of disorders intermediate between Pick and other degenerations, and goes on to criticize Spatz's theory of the "systemic atrophies." He holds that each of the disorders included within it is due to a distinct gene. Intermediate forms linking the separate disorders are due to the fact that each gene has a central locus of expression in the C.N.S. and a more vaguely defined peripheral area where its effects may occasionally extend owing to the operation of contingent factors. In this way an overlap in the manifestations of different genes may result. This is, of course, only a pictorial rationale of the present system of classification of the degenerative disorders. Becker is wrong in stating that there is no evidence for multiple allelomorphism in the heredo-degenerative disorders of the C.N.S. He is presumably unfamiliar with the work of Haldane (1941a). Polemics between those affirming the unity and those insisting on the diversity of these diseases arise from the fact that genetic and clinical methods of classification may cut across each other (Roth, 1948). At present a subdivision

based on clinical criteria is generally more convenient. It must be remembered, however, that "intermediate forms" offer a suggestion of some fundamental factors common to the separate clinical disorders concerned, and these may prove of importance when we know more about the physiopathology of the systemic degenerations.

Two new pedigrees of Pick's disease have been published by Malamud and Waggoner (1943). In one family two cases in sibs were probably transmitted through the mother. Fifteen members in four generations of the second family were thought to have been probably affected. A single dominant gene was, therefore, responsible for the disease in each family. This is in accordance with previous accounts of inheritance of the disorder. In a paper by Mallison (1947a), to be reported more fully below, a dominant gene seemed to be responsible for two cases. An interesting pedigree of a third family is reproduced, showing five cases of Pick's disease in two generations. The family also contained one example of senile dementia and a variety of other neuropsychiatric disorders.

One of the pedigrees reported by Delay *et al.* (1945a) contained a sibship of three. The disorder was probably transmitted through the mother. Age of onset was remarkably uniform in all four cases. The family was also noteworthy for the presence of a pronounced digital, lingual and peribuccal tremor in each individual affected by Pick's disease.

An investigation of 150 cases of cerebral atrophy in old age has been carried out by Mallison (1947). They included Pick, Alzheimer, Parkinsonism, G.P.I., chronic psychoses, cerebrovascular disease, and a condition of obscure aetiology not fitting into any of the conventional categories and consisting of a premature state of intellectual and emotional decrepitude ("Versagenszustand"). He claims to have observed a clinical syndrome which covered the early symptomatology of most cases; its leading features were exaggeration of certain personality traits, depressive bouts, impairment of initiative and concentration and diminished vitality. Air studies indicated that in all groups atrophy showed a selective preference for the frontal, temporal and parietal lobes, while the occipital lobe was exempt. He suggests that one common pathogenetic factor in these various disorders was the vulnerability of these phylogenetically recent areas of the cerebrum (*vide infra*, cf. Malamud and Waggoner). The genetic uniformity of senile and presenile dementia and general paralysis postulated by Patzig (no reference given) was, he thought, another factor determining similarities between the different clinical groups.

That cerebral atrophy links certain paranoid psychoses to the "abiotrophies" has been suggested by Delay (1945). The views of this author as well as Mallison are based to a considerable extent on findings on air encephalography and will be referred to again below. A number of separate disorders appear to be contained in the entity that has come to be known among neurologists as "cortical atrophy." Epilepsy of late onset is the usual presenting symptom, and there are other features strongly suggestive of cerebral tumour (*vide infra*). Jackson mentions among the aetiological factors which make their contribution, atrophy of the Pick and Alzheimer type, Schilder's disease,

atrophy due to circumscribed areas of encephalitis following specific fevers, thrombosis of a cortical vein, cerebro-vascular disease and arteriovenous fistula. However, it is probable that even when due regard is given to these factors, there remains a group of cases whose origin is obscure. Among twenty-eight cases of cortical atrophy in adults collected at a neurosurgical centre within a few years (Fleminger, 1946) there were twelve cases under sixty years of age in which head injury, infection, hypertension and arteriosclerosis were held to be excluded as causes of the disorder. Psychological and psychiatric data are scanty in the relevant literature, so it is not possible to judge from the reports whether any of these cases could have been examples of early presenile dementia, but Fleminger states that though dysphasia was common, "mental change suggesting dementia" was absent. Jackson's cases, on the other hand, impressed him as intellectually dull, and as having defects of memory and concentration. In his material the onset of the condition was usually between thirty and fifty. Other clinical features he mentions are pyramidal signs, reduced sensory perception and, in 25 per cent. of cases, a visual field defect. Headache occurs in half of the cases and has hypotensive qualities. Epileptiform attacks commonly of Jacksonian kind are usual, and are followed, after a period, by paresis of a limb or hemiparesis. C.S.F. pressure is low, but serology is normal. It will be evident from these reports that there is a relatively common condition of presenile cerebral atrophy which may not be covered by the conventional psychiatric categories and which deserves detailed neurological, psychiatric and psychological study.

(b) *Clinical Aspects.*

The clinical picture in nine cases of Alzheimer's disease and one case of Pick's disease has been analysed by Stengel (1943). He emphasizes the over-activity in Alzheimer's disease, which partakes of some characteristics both of the iterative behaviour of obsessionals and the hypermotility of the hypomaniac. Extreme emotional instability on a background of euphoria or distress is typical. The dysphasia involves expression as well as comprehension, but its specific features derive from an interaction between the general impairment of intellectual function, to which palilalia, perseveration and echolalia may be attributed, and the localized speech defect of auditory type. Commands directed at the patient's own body were often comparatively well executed. Some apraxia was present in all patients, though disabilities under this heading were difficult to disentangle from those of an aphasic and agnosic kind. Stengel draws attention to the similarity between the tension, motor unrest and stereotyped utterances of these patients and those suffering from involutional melancholia. These features differentiate the disorder from Pick's disease, in which apathy and inertia are typical.

Inertia is not necessarily present in the early stages of Pick's disease, while in Alzheimer's disease the patient may at times appear emotionless, dull and apathetic, owing to diminished spontaneity and a raised threshold for attention and affective response. This latter condition, called "Affektschlummer" by German authors, suddenly changes to tense anxiety-laden purposeless hyper-

activity in response to strong stimuli (Leuchtenberg, 1942). Interacting and overlapping focal disturbances ("Verwaschene Herdstörungen"), in which the separate components are sensory aphasia, ideokinetic apraxia, agraphia and gnostic disturbances, produced by massive parietal lobe lesions, are pathognomonic for Alzheimer. Leuchtenberg (1942) denies the existence of the parieto-occipital form of Pick's disease. Bagh's findings (*vide infra*) contradict this view. However, there can be no doubt that when Pick's disease attacks the parietal lobe alone, differentiation from Alzheimer's disease is impossible, at any rate until the frontal lobes have also been involved.

Edwards (1943) has briefly reviewed the literature dealing with the diagnosis of presenile dementia. He is sceptical about the possibility of differentiating Alzheimer from Pick's disease. With Latham (1943) he has described a new case of Alzheimer and the pathological findings. A case of Pick's disease fully investigated by Malamud and Waggoner (1943) showed defective abstract behaviour, while learned and concrete material was retained in the early stages. They explained his disabilities as due to impairment of categoric thinking.

From their pathological investigations Malamud and Waggoner conclude that Pick's disease is a systemic degeneration of the phylogenetically youngest areas of the brain. Discrepant with this was extension of the disease in their cases to some primordial fields, such as the temporo-polar and orbito-frontal areas. Also against the view expressed by these authors is the work of Bagh (1942), who reported on the anatomical findings in thirty cases of Pick's disease. The insula, a phylogenetically old area, was always severely attacked. In his material atrophy was predominantly frontal in six, temporal in eleven, fronto-temporal in thirteen, while nine cases also showed parietal involvement. Degeneration of the striatum, especially the caudate nucleus, was severe in eight cases. In the substantia nigra advanced atrophy was apparent in eight, while the fronto-pontine tract was affected in fifteen cases. Bagh holds these extrapyramidal lesions responsible for the loss of involuntary movements and abnormalities of gait towards the later stages of Pick's disease. Hartmann (1944) studied the retrograde changes in the thalamus of two cases of Pick's disease. He concluded that the anterior and dorsomedial nuclei project on to the granular frontal cortex, and that the second and third temporal convolutions have no thalamic connections. He speculates on a possible connection between degeneration of the dorsomedial nucleus and some features of Pick's disease, such as apathy and inertia. Since this degeneration is secondary to atrophy of the granular cortex of the frontal lobes, however, such an explanation would appear to be superfluous.

In a fully documented paper Mallison (1947) reports on twenty cases of Pick's disease studied in some detail. The diagnosis was confirmed by autopsy in twelve cases. Atrophy confined to a single lobe was rare. It was frontal only in six cases, frontal, parietal and temporal in five, parietal and temporal in one case. Asymmetrical atrophy was the rule, predominantly left-sided in eleven, right-sided in two, and equal on the two sides in only seven cases. The occipital lobes were spared in each case. Ventricular dilatation was observed in air studies in sixteen cases. The age of onset was in the sixth decade in ten cases, the fifth in three cases, the fourth in four cases and the

third in three cases. Most patients were seen some time after symptoms first appeared. Progress was slow in the majority, but seven showed acute deterioration. The early symptoms are well described. Among them were disinhibition in conduct and exaggeration of certain emotional traits. Intellectual and mnemonic deterioration appeared much later. A new early symptom is described. It consists of a sudden interruption in the execution of habitual automatized activities, such as use of a familiar implement, orientation in well known surroundings, or explaining the meaning of a simple word. At first this defect is transient. Later it becomes constant and, according to Becker (1948), who has also observed it in his cases, develops on the motor side into a sustained apractic defect. There is no impairment of consciousness, but a sudden helplessness in a well-known situation.

Spontaneous speech had completely disappeared in one case of Pick's disease (Delay, 1944a), although tests showed no aphasia. The disorder was attributed to a general depression of psychomotor activity.

Parkinsonism is a rare development in Alzheimer's disease, and in the few cases reported the symptoms of cortical atrophy have appeared after those resulting from striatal involvement. The reverse sequence was seen in a case reported by Leavitt and Lewey (1945), which had an exceptionally long duration. During the last three years of life she was in decerebrate rigidity. At post-mortem there was marked hydrocephalus and severe atrophy in cortex and basal ganglia with extensive fibrillary change and abundant plaques. A case of predominantly hemilateral cerebral atrophy due to Pick's disease was reported by Balado and Pedace (1945). A similar possibility was suggested by one of Ostergaard's cases. Pick's disease combined with parenchymatous cortical cerebellar atrophy is described by Buchanan, Overholt and Neuburger (1947).

(c) *Special Methods of Investigation.*

(i) *Air studies.*—Air encephalography as an aid to the diagnosis of presenile dementia has been used by Mollaret and Messimy (1943), Delay (1944a and b; 1945a and b), Ostergaard (1945), Jackson (1946) and Mallison (1947a and b). In most cases of Pick's disease predominantly frontal accumulations of air have been reported, but in a case reported by Delay (1944b) atrophy was more marked in the parietooccipital than in the frontal region, and this was in accordance with the clinical findings. In Alzheimer's disease air usually collects diffusely over the whole cortex.

The interpretation of an abnormal air encephalogram in middle or old age may present considerable difficulty. Senile dementia and brain injury may produce appearances indistinguishable from presenile dementia, and in cerebral arteriosclerosis asymmetrical atrophy is often seen (Ostergaard, 1945). Again, schizophrenia is said by Ostergaard to give normal findings, but Delay (1944b) describes one case of schizophrenia with fronto-parietal atrophy on the left side, a paraphrenic of sixty-nine with frontal atrophy, and a case of "psychose hallucinatoire chronique" aged fifty-four with diffuse atrophy. In another case of Delay's (1945b) post-mortem failed to confirm atrophy revealed by air

studies. This author has also observed ventricular dilatation in a case of agitated melancholia, while his findings on air study in one hundred and thirty cases of paranoid psychosis have led him to believe that some of these conditions, with an onset simulating schizophrenia, belong to the "abiotrophic" group.

It is pertinent to ask what is known of the air encephalogram in healthy old men. In a careful and authoritative study Heinrich (1939) has shown that there is a progressive enlargement of the ventricles and cerebral subarachnoid space with age. This proceeds slowly between adolescence and middle age, but at about sixty a more rapid growth in size begins and the ventricles are also transformed in shape. Mallison's findings (1947) in one hundred and fifty cases with various conditions (*vide supra*) are instructive in this connection. Subarachnoid collections of air were observed in every case. Ventricular dilatation was recorded in 76 per cent. of cases, including ten of twelve cases of G.P.I., four of eleven cases of chronic psychoses, three of five cases of Parkinsonism and twenty-six out of thirty-two cases of cerebrovascular disease. With abnormalities shared by such a variety of disorders one suspects that normal variation with age in the size of the ventricles and subarachnoid spaces may have contributed to the results. It is significant, as pointed out by Mallison himself, that the preponderance of left-sided atrophy in a high percentage of his material should have been recorded by Heinrich in approximately the same proportion of his normal group. Mallison emphasizes that an abnormal air encephalogram is not by itself diagnostic, but holds it may give information of value, especially when a subarachnoid collection of air is circumscribed. In Jackson's view (1946) there are two findings which indicate definite abnormality. These are accumulation of air over the parietal cortex, especially if exposures are made with the patient in the horizontal plane, and visualization of the outline of the third ventricle in lateral view. Summing up, it may be said that air encephalography may give useful information in the mental disorders of middle and old age, but must be weighed with caution in relation to the clinical findings. Pictures suggestive of brain atrophy may result from a number of different diseases, but may be due to ageing and have no pathological significance.

(ii) *Electro-encephalography*.—Mollaret and Messimy (1943) report diffuse low voltage fast activity in a case of Pick's disease, while Delay (1944c) describes absent alpha activity in the parieto-occipital region, corresponding with the side of atrophy. In another case of Pick (Delay, 1944a), however, the E.E.G. was normal, while Lovell (quoted by Ostergaard) found no changes in fourteen out of twenty cases, those in the remaining six being slight and quite uncharacteristic. A case investigated by Polatin *et al.* (1948) likewise showed mild insignificant abnormalities. The findings of Hill (1948) are more definite and have practical value. In sixteen cases of presenile cortical atrophy the E.E.G. was abnormal in eight, four of these showing severe abnormalities. It was in the acute phases of the disorder that the record tended to be abnormal, even focal abnormalities disappearing as confusion and clouding of consciousness subsided. In the chronic stage a slowing of the alpha rhythm to 6-8 c/s was observed.

6. MISCELLANEA

New cases of Jakob-Creutzfeldt disease have been described by Dimitri and Aranovich (1945), Stengel and Wilson (1946), and Meyer and Nevin (1947). Unusual pathological features in one of Stengel and Wilson's cases were the presence of numerous senile plaques, involvement of the substantia nigra, and changes in the peripheral nerves. Pointing to the similarity of the spinal cord changes to those in subacute combined degeneration they suggest that the condition may be a deficiency disease. Meyer and Nevin (1948) drew attention to the many similarities between the pathological changes in the C.N.S. seen in the heredo-degenerative disorders of the nervous system and those in old age as described by Gellerstedt.

Chronic subdural haematoma is one of the most difficult diagnoses to establish, especially in old age. Abnormal neurological signs are often of a subtle kind or even absent (Abbott, Due and Nosick, 1943), and the C.S.F. findings may be equivocal. Fleiss (1946) reports an unusual case of recurrent mania. In two attacks marked improvement followed evacuation of a subdural haematoma. In two other attacks no exploration was carried out, but recovery occurred spontaneously. On one occasion, during an attack, exploration failed to reveal an haematoma. The subject is of some importance, as Allen, Moore and Daly (1940) in an analysis of 3,100 consecutive cases of sudden death in mental hospital patients found 245 examples of subdural haematoma, an incidence of 7.9 per cent., though only in thirty-five was the haematoma judged to have been the primary cause of death. In the clinical picture fluctuations from somnolence to clear consciousness are often seen, and unequal pupils, cranial nerve palsies, bradycardia and slow respiration may occur. Signs of increased intracranial pressure, Jacksonian or generalized fits, mild asymmetrical pyramidal lesions or paralysis may appear, but the responsible lesion is notoriously difficult to localize, and this itself should raise a suspicion of the disorder.

10.58 per cent. of all paretics admitted for the first time to New York State hospitals between 1932 and 1941 were over sixty (Arieti, 1945). Such a figure fully justifies Arieti's plea for C.S.F. examination in all psychotic patients over sixty. In the material he studied length of incubation period followed Megendorfer's rule, its duration being in inverse relation to the age at which infection occurred. Intellectual defects tended to dominate the clinical picture, often constituting the only symptoms. Euphoria and grandiose delusions were more common than in senile psychosis. Neurological signs were often indefinite. A pathological study of six cases led him to suggest that (a) neuro-syphilis may be an inhibitory influence on senile changes, while the latter may stimulate neurosyphilitic inflammation, and that (b) neurosyphilis may accelerate the cerebral arteriosclerotic process, but the latter, on the other hand, diminishes inflammation.

The work of Einarson, Neel and Strömrgren (1946) suggests that cases of disseminated sclerosis of late onset are often examples of Schilder's disease. Diminished penetrance of a gene, otherwise manifested as Schilder's disease, may lead to familial spastic paraplegia, usually accompanied by mental change late in life. The data published by these authors, and those they quote from

other workers, offer a suggestion that one mode of transmission in Schilder's disease may be by a partially sex-linked recessive gene. This is of interest in view of Haldane's demonstration that this form of inheritance operated in familial spastic paraplegia.

SUMMARY.

It will be seen that we are somewhat nearer to understanding the biological derivation of ageing, and work is in progress which should eventually tell us something about the relative contribution of humoral factors and of a breakdown in the internal metabolism of cells in the process. Such problems, seemingly remote from psychiatry, are, in effect, of vital importance; a deeper understanding of mental disorder in old age is conditional upon an extension in our knowledge of how and why decrement of mental and physical vitality occurs in old age. The significance of the ageing of the population in most civilized countries has been brought home with special emphasis to psychiatry in a number of studies on the incidence of old-age psychosis. The figures brought to light by such investigations issue a warning that a reorganization of psychiatric services may be required to accommodate an increasing number of old patients. It is probable, however, that too pessimistic a view has been adopted on the basis of some of the figures, as evidence has also appeared that the incidence of mental disease in the old is strongly influenced by social factors which are subject to modification.

That the physical and psychological factors in the causation and treatment of mental disorder are inseparable has been re-emphasized. In this, as in other branches of psychiatry, a gradual *rapprochement* with general medicine is developing, which augurs well for their relationship in the future. On the descriptive side some interesting facts have emerged about bodily changes and the modification of conventional physical signs in the old, but richly documented accounts of the natural history of old-age psychosis are still lacking in the literature. It is a truism that accurate and detailed clinical description is the basis of psychiatry. There is no doubt that the fullest possible accounts of the day-to-day behaviour and experience of the old mentally sick, as distinct from the usual rendering which spot-lights a brief critical segment of their illness, would add a great deal to our knowledge. There has been a welcome increase in the use of physical treatments, and there is reason to hope that prognoses based on the passive custodial care of the old in the past may soon be confounded.

New methods of investigation have produced some interesting results, but further exploration will be required before the interpretation of these results can be placed on a sound basis. The intellectual deterioration that makes some contribution to the causation and clinical picture of every old age mental disorder has come to be delineated with increasing precision in recent years. However, utilizing the assets of the old has become one of our most urgent social problems, and we need, therefore, to be better informed about the factors which decide that the summits of achievement in so many intellectual and creative workers are not touched until middle life and even old age.

Many investigators in psychiatry, as well as other branches of medicine, have tended to make a sharp distinction between "normal" or "physiological" ageing and "pathological" ageing. Now it is of considerable practical value to distinguish between the old who merely suffer from some decrease in physical and mental efficiency and those who, in addition, have some positive disorder, such as cardiac decompensation or a psychosis. It will be evident, however, that the line of demarcation between the two types of phenomenon is an indistinct one. The difference between them is often attributable to environmental contingencies; exceptional hardship and exertion may serve to transform one into the other. Moreover, as no individual grows old completely free from the cumulative pathological effects of injury and disease, "normal" ageing, in the sense of a purely intrinsic process independent of such influences, is an abstraction. It is true that in a statistical sense one can give "normal" ageing a more precise meaning, but there is some danger in medicine in using the term in this manner, as it is easily forgotten that the phenomena to which it is applied may call for modification by medical means. Thus, a certain degree of dental caries may be normal on a statistical scale of measurement, but the task of medicine is to render it abnormal and ultimately non-existent. In other words, an ideal standard of physical and mental well-being is the only possible yard-stick for the measure of normality valid for medicine. The mental and physical involution that is the fate of most people who live to be old is then seen as one of the most formidable obstacles on the endless path to the attainment of this ideal.

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BORDERLANDS OF NEUROLOGY AND PSYCHIATRY.

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It is proposed to survey under this heading recent work on the impairment of some of the highest cortical functions which are the common concern of the neurologist and the psychiatrist. In addition, work on the psychiatric aspects of head injuries is to be reviewed.

APHASIA, APRAXIA, AGNOSIA

(including Disorders of the Body Scheme).

Any attempt to consider aphasia, apraxia and agnosia separately is bound to fail. They will be dealt with in the above order, but there will be considerable overlapping, which only reflects the interrelationship of these disorders. Research has proceeded along several lines. The approach of the majority of workers has been clinical and psychological. The deep impression that the work of Goldstein, who followed in the footsteps of Jackson, Marie and Head, has made on the younger generation of neurologists and psychiatrists is very obvious in most of the publications. On the other hand, there has been a distinct revival of interest in purely localisatory problems among a group of neurologists. The problem of rehabilitation of aphasics has received considerable attention. Some workers have reported on clinical experimental work, while another field of experimental research has been explored by the systematic study of the effects of electrical stimulation of the cortex on speech mechanisms. Neurosurgery has also contributed interesting observations concerning speech disorders.

The most important addition to the literature in recent years is undoubtedly Goldstein's book, *Language and Language Disturbances* (1948). In this work the author restates the fundamental theories expounded by him over many years. They form the basis of the holistic approach to the study of impaired brain functions, especially of those of the highest level of integration. He views symptoms of brain damage as disorders in the function of the organism as a whole, without losing sight of the significance of the localization of the lesions. He distinguishes four groups of symptoms: (1) Defects of performance, i.e. the negative symptoms of Hughlings Jackson; (2) indirect symptoms, due to the effect of separation of an undamaged area from a damaged one, i.e. Jackson's positive symptoms; (3) secondary symptoms, i.e. those due to the effect which the pathological process in the damaged area exerts on other parts of the nervous system; (4) symptoms which represent protective mechanisms against the effect of impairment of the personality. Individual speech performance, normal and impaired, is according to Goldstein, understandable only in its relation to the function of the organism in its endeavour to

adjust to its environment, and to realize itself as much as possible in the given situation. The contributions of psychology, philosophy, linguistics and the study of normal speech development are critically reviewed. The problem of localization is fully discussed. Only in what he calls the periphery of the cortex is there an exact correspondence between certain sectors of the periphery of the organism and certain cortical areas. All types of language disorder correspond to states of dedifferentiation of language. Goldstein is not an iconoclast. In his classification of aphasia, he builds on the traditional system as established by the classical authors. The most important feature of Goldstein's classification is the central aphasia, i.e., a speech disorder due to impairment of abstract thinking which may be associated with disturbance of either the expressive or the receptive side of language. Thus he distinguishes a peripheral and a central motor aphasia, the former being identical with Broca's aphasia; a peripheral receptive aphasia and the central aphasia proper; an amnesic aphasia and the transcortical aphasia. The central aphasia has much in common with Wernicke's *Leitungsaphasie* (conduction aphasia) to which Goldstein has given a new interpretation. There are excellent chapters on the examination and the treatment of speech disorders. The book contains a collection of illustrative case records.

The problem of localization has been lucidly discussed by the same author (1945) in another publication. He examines the factors which, in addition to the site of the lesion, determine the appearance or non-appearance of certain symptoms.

Goldstein came to the conclusion that the function of the organism could not be understood without the combination of empirical research with philosophical reasoning. Hutton's article (1943) on language and its relationship to conceptual thought is an example of philosophical reasoning. Hutton examines among other problems the concepts of categorical and abstract thinking which Goldstein uses interchangeably. She regards categorical thought as a scientific mode of thinking and points out that there are other modes of abstract thought which do not involve the use of categories. The main part of Hutton's article deals appreciatively with W. M. Urban's (1939) book, *Language and Reality*.

Alajouanine and Mozziconacci (1948) in a monograph on aphasia and the functional disintegration of language advocate an approach similar to that of Goldstein's. They warn against the danger of recent progress in neurophysiology leading back to a narrow concept of localization. They support the view that aphasia is an apraxia of speech and point to parallels between the various levels of speech disorders and those of apraxia. In a number of other articles (1947, 1948) they describe various types of dissociation of the constituent components of speech which they regard as fundamental. In aphasia the effortless use of and the interaction between the automatic and the conceptual components are impaired.

Conrad (1947, 1948, 1949) has concerned himself systematically with problems of aphasia in recent years, both from the psychological and clinical point of view. He has been strongly influenced by Goldstein and V. Weizsäcker whose concepts he attempts to co-ordinate and to combine, but he has

developed views of his own regarding the nature of aphasic disorders. He leans on Sander (1928) who studied experimentally the genesis and disintegration of gestalt experiences. Gestalt is preceded by *vorgestalt*, i.e. a primordial phase of gestalt formation. Conrad relates aphasic phenomena to that phase. He has created a formidable terminology of his own. Borrowing Head's now somewhat obsolete terms, he speaks of epicritic and protopathic impairment of gestalt formation and even regards the concept of *vorgestalt* as the clue for the understanding of unconscious mental processes. Here the author is in danger of overrating the usefulness of the concept. At any rate, Conrad's work opens interesting vistas for detailed researches into the dedifferentiation of higher cortical functions. His structural analyses of various types of aphasia make interesting if not easy reading. The same author also studied problems of localization of various types of aphasia in a large group of brain-injured cases. His views on localization are similar to those of Goldstein.

Zangwill (1946) reported on some qualitative observations concerning verbal memory in cases of cerebral lesion. An impairment of memory span for verbal material and severe difficulties in rote learning were consistently found in cases with language disability associated with focal lesions of the speech areas. These defects may long outlast the grosser aphasic symptoms. The defect of verbal learning in these cases is mainly syntactical. Immediate memory and sentence learning, therefore, have value in detecting very slight degrees of language involvement. Cases of pronounced impairment of general memory have intact verbal memory span, but grossly impaired verbal learning. Substance recall is defective in these cases. Some impairment of verbal learning is common in organic cases irrespective of the nature and localization of the lesion.

The experienced reader will find a number of interesting observations in Nielsen's book (1946), *Agnosia, Apraxia, Aphasia and their Value for Localization*, but also a great deal of old-fashioned "brain mythology." Nielsen continues on the lines of Henschen and Kleist. His confidence in the possibility of exact localization of the various types of disorders is almost unlimited. He does not concern himself with the analysis of these symptoms. Modern concepts of localization are ignored. Nielsen's approach is atomistic. He proposes a physiologic-anatomic nomenclature comprising 87 disorders of the aphasic, apractic and agnostic type, each of them with its respective localization. Several papers by the same author and his collaborators deal with special problems of localization whereby the importance of the homologous area of the minor hemisphere for the recovery of impaired functions is stressed. Amnesic aphasia is, according to Nielsen (1944) due to a lesion of the major temporal lobe. Nielsen and Friedman (1942) studied the effect of lesions within the quadrilateral space of Marie and express the view that destruction of the external capsule causes motor aphasia in these cases.

Needles (1942) reported on observations which seem to suggest that even when it comes to transfer of cerebral dominance in the function of speech as the result of a lesion, both hemispheres continue to participate in that function.

Schiller (1947) investigated 46 cases of aphasia due to penetrating missile wounds. The patients were subjected to twenty standard tests, including

vocabulary, Kohs' blocks and matrices tests. With this test battery "the salient features" of any given case of aphasia can be picked out in about an hour. The mixed nature of most aphasic disorders was confirmed, and so was the commonly accepted gross localization of the lesions underlying the main types of aphasia. Schiller advocates an anatomical classification of aphasia.

Teitelbaum (1943) discusses agnosia, apraxia and aphasia from the point of view of levels of integration. In his opinion agnosia and apraxia correspond to disintegration of functions at a lower level of complexity than aphasia.

Trent (1946) proposes a redefinition of aphasia, apraxia and agnosia with the aid of a terminology adopted from modern logic. He distinguishes three levels of integration above those of sensation and muscle contraction: the syntactic, semantic and pragmatic.

Critchley (1942) made an interesting and original contribution in studying disorders of signalling in trained signalmen which he observed in the Royal Navy. For them the Morse code has become a language of its own. But, as Critchley points out, signal speech differs from spoken language in that it is almost exclusively propositional. The first case reported is that of a naval cadet who puzzled his instructors by his extremely bad spelling and his inability to learn Morse signalling. He was slightly above average in intelligence. The disability is related to congenital alexia and word-blindness. "Signal-aphasia" has also certain features in common with receptive amusia. The second patient was a signalman suffering from a Lissauer type of general paralysis. He showed an executive disability of signalling, probably of an apractic character. The third case, a retired Chief Yeoman of Signals, developed, as the result of vascular lesions, agnostic disabilities (alexia, impairment of the appreciation of the significance of pictures and a minor degree of visuo-spatial disorientation). He showed impaired recognition of flag symbols, while his Morse flashlight signalling was intact. The discrepancy between the preserved latter ability and his difficulty in reading suggests to the author that speech and signals are not identically represented in the cortex. There is a resemblance in that way to the relationship between speech and music. Critchley does not assume that in his cases the disability of reading and transmitting signals is a specific disorder. It is an impairment of an acquired special language, the complexity of which, as a means of communicating symbols, is even greater than that of a foreign language.

Leischner (1943) observed total aphasia in a deaf and dumb person with lesion in the region supplied by the left middle cerebral artery and softenings in the angular and supramarginal gyrus. The aphasia gradually improved and the patient could make himself understood, though with difficulty, in the deaf and dumb language. However, a marked polyglot agraphia, which had formed part of the syndrome from the beginning, remained.

Monrad-Krohn (1947) describes as the "*prosodic quality of speech*" that faculty of language which conveys different shades of meaning by means of variations in stress and pitch, irrespective of the words and the grammatical construction. Besides the intrinsic prosodic character of every language and dialect, there is an emotional and intellectual (propositional) prosody. Clinically, one finds three types of prosodic disorders: (a) the functional, (b) the

organic dysprosody, (c) aprosody and hypoprosody due to brain lesions. The author describes in detail a case of dysprosody following injury of the dominant hemisphere.

Critchley (1947) discussed the relationship of aphasic disorders to individual education and to the command of language. In his experience, poor education, especially with regard to the accomplishment of writing and reading, makes severe and lasting aphasia unlikely. Aphasia seems to be more severe in those who have developed speech to its highest perfection. On the other hand, the verbose, mercurial individual might require a comparatively large and crippling cerebral lesion to silence him.

Alajouanine (1948) investigated the problem of the fate of productive artistic activities, literary, musical or pictorial, after the onset of aphasia. He had the opportunity of observing three eminent artists; a writer suffering from motor aphasia, a musician and a painter with auditory aphasia. In all three cases aphasia spared the personality, especially its aesthetic components. It did not alter their sensibility, their memory, judgment or taste, although the writer and composer were annihilated as to their artistic production. The painter carried on with his art as if nothing had happened. Aphasia, in the author's view, more or less respects the individual total personality.

Penfield and Rasmussen (1949), "in order to set the stage for a study of aphasia" recorded some interesting observations with regard to (a) vocalization as a response to stimulation of the human cortex, and (b) arrest of speech by means of stimulation. Electrical stimulation in a small zone of the central gyrus produced a vowel or arrest of speech. Speech could also be arrested by stimulation of other areas of the dominant hemisphere. Three such areas were found: a Rolandic zone, an extrarolandic frontal and a parietal zone. Speech arrest from the two latter zones did not seem to paralyse any motor mechanisms, but appeared to interfere with the correct choice of words. The authors gained the impression that arrest of speech was associated with interference of certain processes of thought.

Robb (1948) reported on the effect of excision of frontal lobe cortex on speech. No speech defects were observed as the result of prefrontal excisions. Even when Broca's area was excised no permanent loss of speech ensued, but there was post-operative aphasia. Szanthal (1947) failed to observe motor aphasia following almost total excision of that area, but there was amnesic aphasia which he regards as a symptom of frontal origin. Raney, Friedman and Nielsen (1942) studied a case of aphasia following left temporal lobectomy. Spontaneous speech was completely lost and comprehension of spoken language was gravely impaired. The patient was unable to read or write.

Critchley (1948) has written a survey of speech iterations (stammering, palilalia, echolalia and allied phenomena, verbigeration, recurring utterances of aphasics). He recalls Jackson's analysis of some of these phenomena which has thrown light on the problem of the relationship between thought and speech. Critchley quotes some examples of speech iterations in literary art and draws attention to the frequency of iteration in primitive language and in the speech of young children.

Stengel (1947) made a clinical and psychological study of echo-reactions with special reference to echolalia. Echo-reactions do not consist in indiscriminate repetition, but depend on personal rapport. The selectivity of the reactions can be easily demonstrated. They are fundamentally social phenomena based on the mechanism of identification. A tendency of patients with echo-symptoms to complete automatically sentences and actions initiated by the persons with whom they had established contact was observed. The various phases which echolalia undergoes in the evolution and re-evolution of speech were analyzed. The author advanced a new interpretation of echo-reactions in schizophrenics. He examined the formal as well as dynamic significance of echo-phenomena from the point of view of gestalt psychology.

Guttmann (1942) studied 30 cases of cerebral hemisphere lesions in children with a view to comparing the frequency, clinical picture and prognosis of acquired aphasia in children with adult cases. Aphasia was found to occur in this group with the same regularity as in adults. In all cases under ten years, and in some between 10 and 14, the clinical picture is uniformly that of diminished speech production, with dysarthria and telegram style in the recovery period; this applies equally to cases with frontal and temporal lesions. The latter show disturbances of receptive as well as expressive speech. The recovery from aphasia of the purely motor type is surprisingly rapid; most cases recovered within four weeks.

Brain (1945) discussed the evolutionary development of the relationship between speech and handedness, with particular reference to aphasia in cases with lesions of the minor hemisphere and the prognosis of speech disorders in children. He surveys the problem of hemispherical dominance from the point of view of the localization of lesions leading to symptoms of aphasia, agnosia and disturbance of the body scheme. Conrad (1949) reported on aphasic disorders in cases of brain injury in left-handed subjects. Among 808 cases of head injuries, mostly war casualties, he found left-handedness in 5.8 per cent. Only one-quarter of the right-handed patients were aphasic, but one-third of the left-handed. Contrary to expectation, the majority of left-handed cases with aphasia had a left-sided lesion. Left-handedness does not imply dominance of the right hemisphere to the same degree as right-handedness implies dominance of the left hemisphere. Conrad regards left-handedness as an expression of incomplete specialization of brain function.

Hasenjaeger and Poetzl (1941) studied in detail a patient who had Jacksonian fits in the tongue and the left facial muscles with anaesthesia. Gradually a motor aphasia developed, and later still agraphia of a type regarded as typical of parietal lesions. The authors suggest that lesion of Broca's area results in disturbance of the speech rhythm, and that in case of destruction of that area the parietal lobe intervenes. This assumption was suggested to them by the clinical findings in their case which showed a destruction of Broca's area.

Bertha (1942) discusses the mutual influence of homologous parts of the parietal lobe. Mirror-writing of the left hand may arise from interruption of the connections between symmetrical cortical areas. There is a phase in normal development when laterality is still incomplete. During that phase there is a tendency to mirror-writing with the left hand, which is an expression

of the function of the minor hemisphere. Parietal lesions tend to create a similar situation in the adult.

Erickson and Brickner (1943) observed aphasia-like reactions associated with hypnotically-induced amnesias. Amnesia for a specific thought or class of thoughts was suggested. In these cases amnesia also involved certain collateral thoughts not suggested by the hypnotist; e.g. in a patient who wanted to escape, amnesia for that idea was suggested. This patient failed to recognize keys for a day after the hypnotic session. A boy who in hypnosis was told to forget his age was unable, while the amnesia persisted, to read or write the number signifying his age.

Kanzer (1942) found that speech disorders in cases of brain tumours usually start with amnesic aphasia, irrespective of the site of the lesion. In cases where amnesic aphasia appears with or after involvement of the right upper extremity, the anterior part of the brain is usually involved. In cases where amnesic aphasia preceded the above symptoms the lesion was found to be situated in the posterior part of the brain. Amnesic aphasia may be regarded as a disturbance in language due to the disruption of the association pathways between sensory and motor areas, or it may be considered as the result of an early lesion within the common language area.

Riese (1949), studying speech disorders in cases with brain tumour, points out that aphasia is most likely to appear when the development of the tumour is rapid. It can be expected to be absent when the momentum of the tumour growth is small, even if the critical areas are involved. At best it may occur among the late symptoms. The absence of speech disorder, therefore, does not necessarily mean that the critical areas are not involved in a massive lesion of slow momentum.

Riese (1949), in another publication, reports an interesting case of aphasia following brain operation in a scientist. This patient in his aphasia, expressed himself in a poetical language rich in symbols, thus apparently contradicting the rule that dedifferentiation of speech function implies a reduction or loss of symbolic or abstract thinking. Riese points out that this case did not contradict the rule that the law of dissolution must be interpreted and applied individually according to the meaning of the terms of the law in a particular case.

Hemphill and Stengel (1940) described a case of pure word-deafness following head injury. Audiometric examination revealed slight hearing loss. They discuss the position of pure word-deafness with regard to disturbance of auditory perception on the one hand, and typical receptive aphasia on the other. In their case the speech disorder was associated with asymbolia for pain. The significance of this combination will be commented on later in this survey.

A number of authors described transitory aphasia in the course of infectious or vascular diseases. Ornstein (1942) observed motor aphasia during migrainous attacks. Dixon and Roaf (1946) reported on transient motor aphasia, together with signs of meningeal irritation and migraine in a case of undulant fever. Ledoux and Jacquot (1948) described the transitory syndrome of right-sided hemiplegia and motor aphasia in cases of mitral valvular disease.

Stengel and Mayer-Gross (1945) studied disorders of speech in therapeutically-induced insulin hypoglycaemia. They observed a variety of phenomena

during the stages of going into and waking from coma ; isolated dysphasias, echolalia, articulate rhythmic ejaculations occurring together with myoclonic twitchings and primitive utterances associated with choreo-athetotic movements. The articulate ejaculations associated with myoclonisms are due to cortical discharge. They sometimes culminate in the scream ushering in a major epileptic fit. It is suggested that the epileptic cry is always a symptom of cortical discharge. Penfield and Rasmussen's observations on the effect of cortical stimulation (see above) seem to confirm this hypothesis.

Sivadon, Bouquerel and Bodin (1947) observed transitory motor aphasia with hemiplegia following therapeutic insulin coma.

Systematic re-education of aphasic patients is the subject of a number of papers. Bakes (1945) describes two methods ; the first known as the motokinesthetic method, i.e. manipulation of the articulatory organs ; the second, called kinesthetic, consists in tracing the written word with the fingers. Alajouanine and Mozziconacci (1947), in their method of retraining aphasics, aim at stimulating the use of intact automatic mechanisms with the help of pictures, current idioms and completion exercises. Butfield and Zangwill (1946) reviewed the outcome of re-education in 70 dysphasics. The results are considered in relation to the various aspects of language affected and to their severity and aetiology. The most favourable results were observed in traumatic cases and in those whose symptoms were mild and of the executive side. The authors followed in the main Goldstein's methods of retraining, as also did Granich (1947), who wrote a manual on speech disorders as a guide for those engaged in retraining aphasic patients. Granich's book is based on experiences of the U.S. Army Medical Corps. Peacher (1947) reported on the organization of the Speech Clinics in the allied forces. Most of the patients treated in these clinics were dysphasics. Eisenson's book (1946) on examination of aphasia and related disturbances is also intended for the use of the speech pathologist and psychologist dealing with rehabilitation of aphasic patients. It includes a collection of relevant test material. Eliasberg (1947) stresses the social implications of aphasia which have to be foremost in the mind of everybody engaged in remedial work with such patients.

Linn (1947) used sodium amytal by intravenous injection in a group of aphasic patients. In some a dramatic improvement was observed. All the cases were war injuries. The author recommends this treatment as a means of hastening rehabilitation in patients with traumatic aphasia.

Apraxia.—While Liepmann's basic clinical concept of the disorder has remained unchallenged, the interpretation and classification of its various types is still under critical review. Nielsen (1946) speaks of "cortical motor pattern apraxia" instead of motor apraxia. He regards the apractic performance as the functional pattern of the minor hemisphere. Nathan (1947) studied facial apraxia and apractic dysarthria. He described four cases of isolated facial apraxia, one case of facial apraxia associated with apraxia of the left limbs, and one case in which it was associated with apraxia of the right upper limbs. Facial apraxia is often associated with dysarthria, which, in cases of Broca's aphasia, is due to facial apraxia. The localization of the lesion leading to facial apraxia and apractic dysarthria is fully discussed, and it is

pointed out that there is no region of the brain the damage of which will inevitably cause apraxia. The author rejects Liepmann's classification of the various types of apraxia. He points out that the most satisfactory concept of the disorder is that of Hughlings Jackson. Apraxia is par excellence the disorder of the motor cortex which activates purposive movements. Apraxia is due to dissolution of the function of the motor cortex. The various types of apraxia mark the degree of that dissolution.

Domnick (1940) described a syndrome consisting of apraxia of the face, dysarthria and apraxia of the contralateral extremity. Facial apraxia is due to lesions in the base of the anterior central gyrus of either hemisphere.

Meszaros (1942) described as "imitation apraxia" the inability to imitate visually perceived actions while spontaneous movements were intact and actions seen could be described correctly.

Carl (1942) observed an "ideokinetic apraxia of the tongue" in a case with lesion of the supramarginal gyrus. Garabelli (1942) and Teitelbaum (1942) reported on cases of apraxia, with autopsy reports. Brain (1941) described apraxia for dressing in cases with impairment of visual orientation and disturbance of the body scheme. There was no apraxia in any other activity. The patients were unable to relate their garments to their own bodies. Apraxia for dressing is regarded as an ideational apraxia. It is independent of constructional apraxia, though a very similar disorder. Martelli (1947) maintains that every apraxia has an element of agnosia and refers in particular to apraxia of dressing. Hemphill and Klein (1948) found dressing disability associated with spatial disorientation as part of a disorder of a geometric agnostic type.

Constructional apraxia, which is invariably related to spatial disorientation, will be reviewed in the following paragraphs.

Akelaitis *et al.* (1944, 1947) studied 18 cases of epilepsy, in which the corpus callosum had been sectioned in variable degrees, for apractic disorders. In 10 cases the motor aspects of the neurological status were normal before and after the operation. In 3 cases in which the operation had resulted in hemispherical damage a motor type of dyspraxia was found. This was probably based on paresis. In a third group, consisting of 5 cases with evidence of diffuse or focal changes in the brain before the operation, dyspraxia was absent in only one case. The conclusion is drawn that dyspraxia in the subordinate or dominant hand after partial or complete section of the corpus callosum occurs only when damage to the contralateral hemisphere exists.

Falkenberg (1941) described a case with isolated apraxia of the left leg due to tumour of the right hemisphere, involving the corpus callosum.

Teitelbaum, Langworthy and King (1942) expressed the opinion that lesions in various sites can cause apraxia if they destroy essential cortical areas and association pathways. These are particularly vulnerable when the supramarginal gyrus is involved.

Constructional apraxia is usually related to disorder of spatial orientation. It is discussed in papers by Lhermitte and Mouzon (1941), Coenen (1941), v. Angyal (1943), Meszaros (1942) and Faust (1947). In Lhermitte and Mouzon's case "geometric apractognosia" and constructional apraxia were due to an occipital lesion. Constructional apraxia can almost invariably be

found in cases with Gerstmann's syndrome and is often associated with visual agnosia.

Visual agnosia.—Brain (1941) described a case of a 15-year-old patient with visual object agnosia combined with alexia and agraphia, finger agnosia, agnosia for right and left and constructional apraxia. In this case failure to recognize line drawings of objects arose not from inability to form a visual gestalt of the shape, but from a defect in that further mental process by which the shape was identified with the object. Object agnosia is to be regarded as the failure to evoke meanings by a particular sensory channel, not the loss of meanings themselves. Brain discusses critically the well-known case of Goldstein and Gelb. He believes that in the present state of our knowledge any attempt to describe in greater detail the nature of the function lost in visual object agnosia is bound to fail. He drew a rejoinder from Goldstein (1943) who had refuted criticism concerning his observations with Gelb many years ago. Goldstein insists that object agnosia is understandable only as an impairment in that step in the process of perception and recognition where gestalt formation takes place, but he makes it clear that he does not assume a strict division between the processes of perception and recognition.

Bay and Lauenstein (1947) challenge the conception of visual agnosia altogether and maintain that the functions involved in this disorder are invariably perceptual.

Adler (1944) studied the disintegration and restoration of visual recognition in a case of visual agnosia following coal gas poisoning. In addition to a fundamental inability to perceive wholes visually, a disturbance consisting of perseveration of visual attention and impressions was identified. Proper perception and recognition were interfered with by superposition of preceding impressions.

Nielsen and Sanborn (1942) distinguish between visual agnosia for animate and inanimate objects.

Several writers analysed agnostic disorders in cases with diffuse cerebral disease. M. T. Paterson and Stengel (1943) described apperceptive blindness (Pick) in a case of general paralysis of the Lissauer type. The post-mortem examination revealed severe occipital lesions. The symptom is understood as a reaction to a chaotic visual impression of the outer world as it presents itself to patients with a severe general mental disorder, interacting with a visual agnosia. Delay, Neven and Desclaux (1944) described a syndrome consisting of visual agnosia, agraphia, astereognosis, ideatory and ideomotor apraxia in a case of Pick's disease with parieto-occipital atrophy. Hanfmann and Rickers-Ovsiankina (1942) studied the structure of agnostic symptoms in free and controlled situations in a case of post-traumatic dementia. They corroborated Goldstein's observations.

Paterson and Zangwill's studies have proved the value of close co-operation of clinician and clinical psychologist. They analysed the recovery of spatial orientation in the post-traumatic confusional state (1944); they described various phases in this process. Orienting data at variance with one another were commonly reconciled by way of rationalization of various specified types. The part played by a dominant affective attitude in provoking and maintaining

disorientation was noted, as well as the similarity of this mechanism to hysterical and delusional reactions, and to certain features in dreams. Disturbance of visual space perception caused by lesions of the right parieto-occipital area in right-handed patients was the subject of another publication (1944). In their material, visual symptoms were associated with constructional disabilities. There was no disorder of the body scheme as seen in similar syndromes due to lesions of the dominant hemisphere. Defect of spatial analysis in the visual sphere was found to be an important factor in the origin of constructional apraxia. A further detailed study (1945) deals with topographic disorientation in a case with a unilateral cerebral lesion. The relationship of the disorder to concomitant disturbances of visuo-spatial perception, constructional disabilities and disorder of the body scheme was examined.

Pfeffer, Friedman and Wortis (1946) described a case of isolated spatial disorientation due to a vascular lesion following childbirth. The patient reacted to her disability with a severe depression. Bender and Teuber (1947) reported on 12 cases with disorders in the spatial organization of visual perception due to parieto-occipital lesions. In some the disability was limited to a section of the visual field. Two cases showed errors of spatial localization predominantly in the sagittal plane. Both showed teleopsia (illusion of excessive depth) which changed momentarily into pelopsia (illusion of abnormal nearness). The paper deserves careful study, both for the methods employed and for comments on the theory of visual perception.

Faust (1947) studied a case with a penetrating injury to the left parieto-occipital area. The patient showed spatial disorientation with a variety of other agnostic symptoms, all of which are related by the author to impairment of visual gestalt formation.

Wortis and Pfeffer (1948) described a case of unilateral auditory spatial agnosia, i.e. a disability to localize sounds in space. This symptom was associated with auditory sound agnosia while language was intact.

Klein and Attlee (1948) analysed a syndrome consisting of word-blindness, amnesic aphasia and homonymous hemianopia in a case of subarachnoid haemorrhage. The most remarkable reaction of the patient was her ability to interpret words without being able to read them. The opinion is expressed that amnesic aphasia may be responsible for special features of acquired word-blindness.

Stengel (1948) investigated the syndrome of visual alexia (acquired word-blindness) and colour agnosia. No other features of visual agnosia were present in his cases. Writing showed certain abnormalities which were shown to be related to the alexia. Certain features which the colour agnosia had in common with defective colour vision were noted.

Reading disability of a non-agnostic type (dyslexia) was described by Jossmann (1947). The dyslectic starts reading like a normal person, but after the first few words or lines the performance deteriorates gradually until the reading ability is lost. The disorder is due to irregular rhythm of eye movements, the direction of which is sometimes reversed. The symptom is believed to be associated with lesions of the area of the cortex responsible for the automatism of eye movements (*limes parastriatus magnocellularis*?)

It is noteworthy that Paterson and Zangwill (1944), in their studies on disorders of visual space perception, also assume an impairment in the eye movements which they regard as apractic.

Hall (1945) discusses the causes and treatment of congenital word-blindness. He regards it as due to inadequate development of vision. Having been word-blind himself until puberty he advocates methods of treatment based on this theory. It is necessary to acquire synthetic vision by means of analytic vision and association. All words must be analysed and broken down and then be resynthesized by association.

Gerstmann's syndrome of finger agnosia associated with right-left disorientation, agraphia and acalculia has been the subject of several publications. Gerstmann (1940) points out that the syndrome may be primary or secondary, i.e. the residue of a wider syndrome. He regards it as the only disturbance of the body scheme which can be found as the result of a circumscribed cortical lesion. In almost all the cases on record Gerstmann's syndrome was found associated with other symptoms, especially with constructional apraxia or with other disabilities of an agnostic nature. Stengel (1944) described a case in which it was associated with loss of spatial orientation and constructional apraxia. Both constructional apraxia and finger agnosia could be related to the same basic disorder which was also responsible for the loss of spatial orientation, i.e. the patient's inability to relate in space objects which form parts of an organized whole to each other and to himself according to rules acquired by experience. The complex organization of the outer world was replaced by a most primitive one, the only measure of which was nearness. A special feature of the cases was mirror-acting and mirror-writing, which appeared to be the result of an inability to fuse and co-ordinate right- and left-hand activities. In Pettler and Raney's (1942) case there was a combination of Gerstmann's syndrome with spatial disorientation and amnesic aphasia. In Teicher's (1947) case a similar syndrome was associated with a depressive psychosis. In a case described by Guillain *et al.* (1947), Gerstmann's syndrome was associated with a variety of other agnostic disabilities and a partial oculomotor paralysis. Other cases were reported by Pedersen (1946) and Arbuse (1947).

Nielsen (1946) suggests that finger agnosia be subdivided into its elements, which should be studied separately. He breaks it up into a visual agnosia for fingers, a loss of revisualization of and an aphasia for fingers.

Klein and Mallie (1945) observed Gerstmann's syndrome in a case of a right-handed person with a right-sided lesion. Finger agnosia was present in the left hand only. There was also a left-sided hemiplegia with disturbance of sensation. Finger agnosia is regarded as part of a more extensive disorder which results in the hand losing the characteristics of a specific organ.

DISORDERS OF THE BODY SCHEME (BODY IMAGE).

The body image or body scheme (the two terms are used in the literature interchangeably) have continued to be in the centre of interest. The books of Schilder (1935) and Lhermitte (1939) have stimulated a great deal of research on the subject which can profitably be approached from different aspects.

Apart from numerous clinical contributions there have been some attempts to re-examine and re-define the basic concept, which, perhaps by its very vagueness, has become a meeting ground of workers in various fields.

Oldfield and Zangwill (1942-43), in a series of articles, examined critically Head's concept of the schema, its history and its application in contemporary British psychology. They compare Head's original definition with that of Bartlett, who tried to elaborate the notion of the schema into a comprehensive theory of memory. While Head's schemata were defined expressly in the language of physiology, Bartlett's schemata are meant to constitute dynamic organizations of psychological material. The authors believe the concept of the schema to form a significantly novel contribution to psychological theory.

Schilder (1942) discussed the part the body image plays in dreams. In his view every single experience is meaningless unless in relation to the body image, which is also of general importance in symbolization. Whenever body image distortions appear in dreams they are of fundamental significance for the interpretation of the dream. They bear relation to early infantile attitudes concerning the body. In the manifest dream contents one's own body image and that of others are interchangeable. In many dreams the body image appears in an infantile form and symbolically disguised.

Villars Lunn (1948) in his book on the body-consciousness, discusses the body scheme from a variety of angles. The author aims at an investigation into the phenomena of normal consciousness, and he regards it as essential to study normal and abnormal body-consciousness first. The phantom phenomena, the "somato-agnostic disturbances" (anosognosia, etc.), the "somato-sensory disturbances" and Gerstmann's syndrome are fully discussed and partly re-defined. A critical review of the literature is given. A provisional definition of the normal body-consciousness is proposed. The author points out that the various writers dealing with impairment of the body scheme have been using fundamentally different concepts. The main reason for the prevailing vagueness in this field is found in the basic assumption made implicitly by most writers, that a special function of the consciousness may be separated from and described independently of the total consciousness. It is to be hoped that this book, or at least an extract, will be translated into English.

Scott (1948) puts forward a new conception of the body scheme. He attempts to relate the neurological concept with the "schema" of the psychologists and with the ego, imago, external and internal objects as defined in psychoanalysis. He tentatively proposes a new definition: "the body scheme refers to that conscious or unconscious integrate of sensations, perceptions, conceptions, affects, memories and images of the body from its surface to its depths, and from its surface to the limits of space and time." Thus it becomes "a continually changing world scheme." He bases the proposed extension of the concept on embryological, neurological, psychiatric and psycho-analytic considerations. He points to a number of clinical observations which seem to call for a new and extended concept which does justice to the unity of the physical and psychic ego with the external world.

The following articles contain contributions to the knowledge of the body scheme in the sense of the current concept. Arguments in favour of a chiefly

peripheral versus a chiefly central origin of the body image were well presented by André-Thomas (1942) and Lhermitte (1942) respectively. In this country, Riddoch (1941), adhering to Head's concepts, regarded proprioceptive impulses as all important in the formation of the body image and refused to attribute a leading role to visual perceptions.

Imperception phenomena, anosognosia in particular, have played a very important part in the theory of the cerebral representation of the body image. Gerstmann (1942) gave a comprehensive survey of the various forms of imperception. He describes his approach as "clinico-phenomenological." He proposes the following classification: (1) Unawareness of disease. (2) Imperception of hemiplegia, of which there are several varieties; (a) Anosognosia, i.e. complete or incomplete unawareness of disablement, (b) anosognosia with amnesia for or imperception of the affected part, from simple forgetting or non-recognition to obstinate denial of its existence, (c) anosognosia which, in addition to the experience of absence, is associated with illusions, confabulations or delusions referring to the affected limb. Gerstmann proposes to apply the term anosognosia also to non-realization of other defects such as cortical blindness; for the variety (b) he suggests the name autosomatamnesia and autosomatagnosia respectively; variety (c) he proposes to call somatoparaphrenia. He regards the phantom limb as an imperception phenomenon, i.e. non-realization of absence and of experience of possession of a lost part. He distinguishes two further disorders of the body scheme, i.e. autotopagnosia and finger agnosia, which are usually associated with agnosia for laterality. He regards finger agnosia as the only clear-cut disorder of the body scheme proper, while all the others are classed as indirect disorders. Cobb (1947) similarly differentiates between agnosia anosognosia and amnesia for limbs. He reports on a case in which amnesia for the left limbs developed into anosognosia.

Hemphill and Klein (1948) distinguish two types of imperception phenomena: unawareness of the defect, and neglect of or amnesia for the defective member. Loss of perceptive functions is the most important factor in the neglect phenomena. It leads to defective realization and inability to construct an image of the affected part. There is in the writers' view insufficient evidence to suggest that the non-dominant hemisphere is of greater importance for the body scheme and its defects than the dominant hemisphere. General lowering of cortical function is regarded as an important factor in the origin of anosognosia.

Rubinstein (1941) described the phenomenon of "imperception for the position of the eyelids on one side" which forms part of the syndrome of imperception for one-half of the body. In one of his cases the syndrome was restricted to the eyelids, and in the three other cases it was most pronounced on the eyelids. The symptom is regarded as a disorder of the body scheme.

Nielsen (1946) proposes to distinguish between the anatomical and the physiological body scheme and their respective disturbances. In the disturbance of the anatomical concept, the patient forgets parts of the body or has distorted ideas about them. In the disturbance of the physiological concept his awareness of, or his ideas about the functioning of parts of his body are lost

or impaired. These two groups of disturbances, which the author considers fundamentally different, are subjected to further subdivisions. Nielsen's differentiation can hardly be regarded as fundamental.

Sandifer (1946) lays stress on the co-existence of clouding of consciousness with anosognosia. The latter disorder is believed to be predisposed by disorders of space perception. A distinction has to be drawn between awareness of personal and of extrapersonal space which may occur together or separately. The affective element also plays a part in the production of anosognosia.

Redlich and Dorsey (1945) observed denial of blindness in six cases with cerebral disease. All cases showed at least a moderate degree of intellectual impairment and a tendency to confabulation. The authors regard imperception to be due to lesions involving the connections between visual cortex and thalamus which form a reverberating circuit. By the interruption of that circuit the conscious representation of the body and conscious experience of the sensual sphere are altered.

Zillig (1941) and Lundquist (1943) observed cases with anosognosia associated with lesions of the dominant hemisphere. In Zillig's patient the symptom was associated with motor aphasia, in Lundquist's case with auditory aphasia.

Friedman and Nielsen (1942) observed three cases with illusion of absence of a limb and loss of emotional expression on the side of the lesion. They believe that the syndrome may be due to a deep lesion close to the thalamus. Halloran (1946) found unawareness of a paralysed limb in a case with subdural haematoma. He believes this to be the first case where this symptom has been caused by a purely cortical lesion.

Wortis and Dattner (1942) reported on a case with the delusion of absence of a paralysed limb. Another limb with certain characteristics of a phantom had taken its place. The patient declared that she had found a strange arm lying in her room and had sewn it on. There was no general impairment of cerebral functions, and the authors regard a focal mechanism to be responsible for the symptom.

Roth (1944) described a case with anosognosia for hemiballism. Another case showed consecutive development of anosognosia for blindness and for the left-sided paralysis, and later autotopagnosia. Thompson and Friedman (1946) reported a case with autotopagnosia and "simultan-agnosia," associated with a paranoid psychosis.

Stengel and Steele (1946) described two atypical cases with imperception of disability. The first was a patient who denied his blindness, which was due to primary optic atrophy from tumour of the base of the frontal lobes. The second patient was suffering from syringomyelia and hydrocephalus, and was unaware of his paraplegia during a psychotic state. Some of the features of the psychotic reaction could be related to the physical disability and its denial. The writers discuss the clinical and pathological constellation under which imperception phenomena may arise.

Roth (1949) observed two cases of anosognosia for hemiplegia, one associated with a partial Gerstmann syndrome. In both cases the lesions were situated in the parietal lobe of the minor hemisphere. Anosognosia of

hemiplegia is regarded as being independent of generalized intellectual impairment. The author discusses points of similarity between anosognosia for hemiplegia and depersonalization.

Similarities between disorders of the body image due to focal or diffuse brain lesions and those observed in neurotic and psychotic states without known organic basis were first studied by Schilder and Lhermitte. Roth (1947) discussing the relationship of neurology and psychiatry regards the defects of the body image common to neurological and psychiatric conditions as an example of the mutual aid which the two branches of medicine can give each other. However, he points to the limitation of that aid. Neurological knowledge has helped in understanding the form and content of the psychiatric symptoms, but has failed to illuminate the aetiology and psychogenesis of the functional disease.

Teitelbaum (1941) told two hysterical patients under hypnosis to forget everything about their body after awakening. The post-hypnotic suggestion produced disturbances in body recognition not unlike those observed in organic cases. They also resulted in a number of associated disturbances of right-left orientation, recognition of objects, calculation and in constructional apraxia. He concludes from the development of these associated disturbances that there is a psychogenic connection between the knowledge of one's own body and these functions, and that the knowledge of one's own body can be disrupted by means of post-hypnotic suggestion.

Brown and Goitein (1943) examined 700 drawings of the "body image" carried out by 250 normal persons with eyes closed. They found five distinctive types of elaboration and presentation (with subtypes of combination). These patterns agreed with an equal number given by five groups among various psychoses.

Bychowski (1943) studied the distortions of the body image arising from psycho-dynamic factors. He considers disorders of the body image "the generating trouble in involutional depression and schizophrenia." By way of the mechanism of projection they are elaborated in hallucinations and delusions.

Pottier (1944) described disturbance of the body image in a case of chronic hallucinatory psychosis. There was the feeling of disappearance of the body and its projection into another person (asomatognosia and heautosopic hallucination according to Lhermitte).

Flescher (1948) in a psycho-analytic study on "neurotic disorders of sensibility and the body scheme" advances a biological hypothesis about neurotic pain and anaesthesia. They are to be regarded as archaic reactions to instinctual danger. The ego withdraws its cathexes from the individual's physical boundaries and resorts to a life-saving physical reduction. In this process neurotic pain corresponds to the experience of (unconsciously hallucinated) separation, as mutilation of the body scheme and anaesthesia correspond to the accomplished severance. Pötzl, many years ago, referred to the analogy between the phenomenon of autotomy in lower animals and certain features of anosognosia.

Asymbolia for pain.—Schilder and Stengel (1928, 1930, 1931) described under this name the absence of a normal withdrawal reaction to pain and

threatening stimuli without impairment of perception. In some of their cases they observed a paradoxical reaction, i.e. the patients instead of withdrawing from the painful stimulus appeared to offer themselves to it.

The cases in which the symptom was observed first had in common a lesion in the supramarginal gyrus of the dominant hemisphere. The authors, in their early communications, referred to similarities between this symptom and abnormal reactions to pain observed in psychotic states, especially in catatonia. Schilder (1937) regarded the phenomenon as an expression of an inability to relate the experience of pain and threatening stimuli to the body image. Stengel (1940) observed asymbolia for pain in a case of pure word-deafness described together with Hemphill, and later (1943) in a case of Alzheimer's disease where the symptom was associated with a severe receptive aphasia. He regarded it as important for the understanding of asymbolia of pain from the biological point of view, that the symptom is almost invariably associated with some kind of word-deafness. He pointed out that receptive aphasia as well as asymbolia for pain represent an impairment in the normal response to external stimuli, the appreciation of which is vital for integrated human behaviour.

Asymbolia for pain was referred to in the discussion of cases with insensitivity for pain (Kunkle and Chapman, 1943) and of "congenital universal indifference to pain" (Boyd and Nie, 1949). Rubin and Friedman (1948) observed asymbolia for pain in 4 cases, all with lesions with localization similar to the cases of Schilder and Stengel. The patients showed extinction phenomena for tactile and visual stimuli, as well as disturbance of the body scheme, such as finger agnosia and autotopagnosia. The authors advance the hypothesis that in these cases the integrating role of the parieto-occipital area of the dominant hemisphere has been impaired, resulting in a new behaviour pattern, characterized by loss of reaction to nocive stimuli. The pattern of the applied painful stimulus is so altered that it can be obliterated by any concomitant enteroceptive impulses, such as those coming from the viscera, the somatic peripheral receptors and elsewhere in the neuraxis. The authors regard asymbolia for pain as an extinction phenomenon.

PSYCHIATRIC ASPECTS OF HEAD INJURY.

A considerable amount of research work has been done since the late E. Guttman reviewed this subject in the first edition of *Recent Progress in Psychiatry* (1944). During the war the practical need for a thorough study of the symptomatology and therapy of head injuries brought together neurologists, neurosurgeons, psychiatrists and psychologists, and the co-operation has continued since. In no other field of common interest has the importance of the psychiatric approach and the active help of the psychiatrist been more highly appreciated by his medical and surgical colleagues. The advance of knowledge which has resulted from that co-operation is reflected in the gratifying results of rehabilitation and treatment of patients with head injuries, and there are clear indications that invalidism from head injury has been much smaller after the second than after the first world war. Work carried out in recent years has consolidated and expanded knowledge collated in the last survey, as well as advancing some problems of fundamental research. Most of the

papers reviewed in this survey come from U.S.A. and Great Britain, where the psychiatric aspects of head injury have been studied more widely and thoroughly than anywhere else. The number of French contributions is small, and their orientation mainly neurological. The keen interest that workers in the English-speaking countries have been taking in the impact of the trauma on the personality structure reflects the great importance accorded to the study of the personality in these countries. It is noteworthy that in the German literature on head injuries published during the war and after, no similar trend can be observed.

For those who want to study all the aspects of head injury, Brock's book which appeared in a third, revised edition (1949) remains indispensable. The volume *Trauma of the Central Nervous System* (1945) also contains much valuable information. Merritt (1943) and E. Guttmann (1944) reviewed most of the work on psychiatric aspects of head injury published between 1938 and 1942. The following is a report on work published since. Like the previous review, this survey will be mainly concerned with closed head injury.

Jefferson (1944) found a 5 per cent. all-over mortality rate for persons with closed head injuries admitted to the neurosurgical centres in Great Britain. Most cases recover more quickly than is usually assumed and taught. If the absence of laceration of the brain has been ascertained by lumbar puncture, treatment should be conservative. The post-traumatic syndrome is to be regarded as neurotic when no blood is found in the C.S.F. Jefferson sees the key to many difficulties in the use of the psychiatrist, not so much as a therapeutic agent, but as a diagnostic colleague. It is important to get the patients up as early as possible and not to permit their discharge until they feel well.

The investigations into the sequelae of head injuries carried out by Denny-Brown and his team at Harvard represent a remarkable piece of team-work. They analysed 200 consecutive civilian admissions of head injuries to the Boston City Hospital between the ages of 15 and 55, excluding vagrants and alcoholics. All features of the head injury were studied in relation to the ensuing disability. Denny-Brown (1945) reported on some aspects of these investigations. Complaints directly referable to structural damage were found in only 16 cases. Eighty-one complained of headaches, 63 of them for longer than two months. Sixty-eight complained of dizziness. The post-concussional syndrome was present in 30 cases and persistent intellectual defects in only 2. Personality changes were found in only 7 patients. One hundred and seventy were absent from employment by reason of their head injury. Of these, 42 returned within a week, 71 within a month, 20 within 2 to 3 months, 9 within 6 to 9 months, 5 were still not fully employed after 9 months. Neurotic and psychopathic pretraumatic personalities were, in this group, returned to occupation earlier than the average of those judged normal. There was a very small correlation between pretraumatic psychiatric abnormalities and post-traumatic mental symptoms. Of 60 with the latter, 57 per cent. had a positive pretraumatic psychiatric history, whereas of 123 who did not develop such symptoms, 50 per cent. had such a history. Blood-stained C.S.F. within 2 days after the injury had a high correlation with disability. Mental symptoms of any pretraumatic kind were highly correlated with disability. Of those with such

symptoms, only 53 per cent. were back to full occupation within two months, and only 76 within 6 months. Of patients without such symptoms, 95 per cent. returned to work within 2 months and 100 per cent. were back within six months. Anxiety was the most prominent among mental symptoms. The circumstances of the injury, the duration of disturbance of consciousness and the environmental factors in convalescence were of the greatest importance. Environmental factors appear more important in accounting for disability than factors indicative of severity of injury. Psychiatric control of the effect of these factors has to be regarded as the most important part of the treatment of these patients.

A. Adler (1945) subjected the same material to a further analysis. Pre-traumatic factors having a high correlation with post-traumatic mental symptoms were advancing age, the married status in men, certain national stocks, certain occupations, the type of injury and pretraumatic symptoms based on anxiety. Prolonged duration of headaches and dizziness was associated with a high incidence of mental symptoms. The post-traumatic neuroses of all but 3 of the 26 previously normal patients conformed to the picture of anxiety neurosis. In another contribution (1945a) Adler points out that the circumstances of the accident are of importance for the development and type of psychogenic disorders, terrifying events having a greater incidence of neuroses than everyday injuries. The author proposes to call neuroses following such events (e.g. disastrous fires, etc.) "fear neuroses," while she regards the neuroses following head injury as "conflict neuroses." Only in the latter type is psychotherapy called for, while in the former, rest and sedation usually suffice.

Kozol (1945, 1946), another member of the Harvard team, reports on the observations which led to the rather unexpected statement that, in their material at least, there was little, or no correlation between pretraumatic personality and the liability to post-traumatic mental symptoms. Other investigations carried out on the same material are the psychological studies by Ruesch and Moore (1943) and by Ruesch (1943). They are to be reviewed later in this survey.

Denny-Brown (1943) points out that the post-concussional syndrome does not appear until the patient is fit to attempt mental and physical exertion. It is a reaction which occurs whenever he attempts something beyond the limit of his power of cerebration. It can occur as a pure psychoneurosis following trivial head injury in patients who had been liable to neurotic reactions previously. The post-concussional syndrome is a reaction to circumstance. The underlying failure may be psycho-neurotic or a remainder from the injury, or a combination of both. There is a close similarity between this syndrome and the so-called effort syndrome. Both may be defined as special forms of nervous reaction following at an interval either threatened or actual damage to the organ concerned.

Allison (1944) classified patients with late symptoms after head injury as follows: (1) Head-conscious neurotic types; (2) post-traumatic epileptics; (3) those with gross neurological signs; (4) those with intellectual impairment; (5) those with personality and character changes.

E. Guttmann (1946) proposed to distinguish five syndromes of the chronic stage following head injury. (1) Largely objective: defect conditions (sensorimotor defect, ideomotor defect, intellectual impairment, personality change). (2) The epileptic syndrome. (3) Largely subjective (the post-concussional syndrome). (4) Psychogenic reactions. (5) Precipitated psychosis of the endogenous type. The author deals chiefly with the second and third syndromes. He estimates that only 20 to 30 per cent. of the patients complain about headaches after convalescence, which means that the occurrence of headaches in patients with head injury in their history is only just significantly higher than in those who never had an injury. From his analysis of 300 unselected cases of civilian head injuries, he came to the conclusion that in most patients who complained of headaches six months after the injury, the symptom was either precipitated by psychological causes, or the patient's attitude towards it was determined by such factors. Guttmann compared the chronic stage of head injury with common neurosis, as A. J. Lewis (1942) had done. His material consisted of 350 service patients. Their subsequent histories showed that the invaliding-out rate during the first years after return to duty was much the same as among the neurotics without head injury. The head-injury group had had less predisposition and less environmental stress than the controls. The head injury balances the relationship between stress and predisposition. Guttmann confirmed the observation made by Symonds and Ritchie Russell (1943) that in the chronic cases the prognosis depends on constitutional factors rather than on the duration of the post-traumatic amnesia. Environmental and psychological factors are important for the establishment of a chronic stage. The material shows two types: (1) Accident neurosis, (2) incidental neurosis. The first can usually be understood as due to fear, shame or guilt. Into the second group fall those cases where the head injury appeared to act as the last straw to a man in a life situation of severe stress.

Wertheimer and Touraine (1947) followed up 250 patients who had to remain in hospital for at least two weeks following head injury. Eighty per cent. had returned to their work, 20 per cent. were not working regularly; 5 per cent. of the latter group were invalids and 15 per cent. have been pensioned off. The periods of temporary disablement in those who had returned to work ranged from three to four months. Among all the patients, headache was found in 48 per cent., vertigo in 36 per cent., subjective visual disorders in 45 per cent., objective visual disorders in 4 per cent. Memory was affected temporarily in 30 per cent. Increased irritability and anger were found in 30 per cent.; traumatic epilepsy was present in 4.4 per cent.; it occurred after latency periods of 8 months to 5 years.

Rowbotham (1949) followed up 1,000 civilian patients who had suffered a closed head injury at least 5 years prior to the enquiry. Of the 430 who replied, 308 were gainfully employed, the rest being housewives and children or people who were for various reasons unemployed. Twenty-nine had not worked again up to the time of the survey. Four of them who had suffered only trivial injuries showed symptoms of severe anxiety neurosis. Only in one case was marked dementia present. Eleven cases had post-traumatic epilepsy. One hundred and sixty-seven patients had been off work for up to 3 months,

58 for 3 to 6 months, 32 for 6 to 12 months, and 22 for 12 months or more. In this series the patients were drawn from the type of injury where the death rate lies between 16 and 20 per cent. The author reports a few representative cases with marked personality changes. The outstanding features in these cases were "negativism" (this term is used for apathy and indifference), laziness, unhappiness, emotional lability, bad temper and intellectual deterioration. To the author it is "abundantly clear that persistent deteriorations in personality and in emotional stability are very common after injuries to the head." This sweeping statement, for which no evidence is furnished, is at variance with the observations of psychiatrists or with psychiatrically informed neurologists and neuro-surgeons. Unfortunately, the valuable case material was not subjected to psychiatric investigations, and it does not appear that the help of a psychiatrist was enlisted in the rehabilitation of these patients. Obviously, the author's pessimistic impression comes from the nature of his material.

Paterson (1942) studied emotional and cognitive changes in the post-traumatic confusional state which show the breakdown of conscious activities in their simplest form. He is not satisfied that these conditions can be understood in terms of disturbance or figure-background relationship only. There is also restriction of the background. It is related to a restriction of the cognitive and emotional attitudes which are responsible for the prominence of certain emotional trends in the post-concussion personality change. The same author (1944) expressed the opinion that the impairment of cortical functions in the post-traumatic confusional state can be related to localized lesions. He found two groups of post-traumatic emotional changes; (a) excessive fear and anxiety, and (b) euphoria and aggressiveness.

Wortis, Herman and London (1945) reported on pre- and post-operative mental changes in 50 proven cases with subdural haematoma due to head injury. Some mental disturbances were found in all patients. They are the most striking neuro-psychiatric findings in these cases. The so-called lucid intervals were found in only half of the group. They should be more correctly designated as periods of return of consciousness which is not always complete. Progression of the symptoms was the most important diagnostic feature. An amnesic-confabulatory picture was common. Post-operational results: 20 cases died, 14 returned to normal work, 15 showed some degree of post-traumatic mental change, the chief defects being impairment of abstract thinking.

Ruesch (1944) studied the diagnostic value of disturbances of consciousness. He reviewed 286 cases with post-mortem examination and examined clinically 49 patients. He stated a number of criteria concerning higher intellectual functions, orientation and reflexes, and proposes with the help of these criteria more objective definitions of coma, semicomá and stupor for the purpose of diagnostic evaluation.

Friedman and Brenner (1945) found in 40 out of 430 patients with closed head injuries prolonged confusion following the injury. In 9 cases the amnesic-confabulatory syndrome of Korsakoff was present over periods ranging from 2 to 44 days. Five of them were chronic alcoholics. The incidence of alcoholism in the group as a whole was 21 per cent. All 9 patients recovered.

They had suffered relatively severe injuries, but many others with equally severe injuries failed to develop the syndrome. Rowbotham (1945) also found a prevalence of chronic alcoholics among those with prolonged confusion. He assumes brain swelling to be responsible for these conditions.

Ritchie Russell and Nathan (1946) discuss the significance of the greater vulnerability of recent as compared with remote memories following head injury. Memory of events cannot be a static process. If it were, distant memories would be more vulnerable than recent ones. The normal activity of the brain must steadily strengthen distant memories so that, with the passage of time, these become less vulnerable to the effects of head injury or other damage. The recall under barbiturate hypnosis, or occasionally in the state of traumatic confusion, of events which cannot be remembered in the state of consciousness may occur as a release phenomenon. The authors report on the results of barbiturate hypnosis in 40 cases with a view to lifting or reducing the traumatic amnesia. In the majority the result was negative. In 12 some additional memory was recovered; in 3 cases both retrograde and post-traumatic amnesia were reduced.

Ritchie Russell (1948) discusses the possible anatomical site of the system of recall in the light of his experiences with traumatic amnesia following head injury. The parieto-temporal area seems to be of importance for that function. He found a much higher incidence of impairment of memory for recent events in cases with the above localization of lesions than in those where other parts of the brain had been damaged.

McConnell (1944) advocates subdural exploration in cases with "prolonged post-operative amnesia," i.e. loss of memory, incapacity to recall recent events, confusion and confabulation. He reports on 6 cases in which this syndrome extended over more than four days following the injury. He found a collection of subdural fluid, bloodstained, yellow or clear, in 5 such cases. The operation resulted in early recovery. The following sequence of events is suggested: The concussion caused a lengthy period of amnesia; during this period a subdural effusion developed and interfered further with cerebral function.

Gurdjian and Webster (1944) discussed the choice of drugs for the control of restlessness following acute head injury. Morphine should be used only when necessary against pain. It causes a consistent and undesirable rise in C.S.F. pressure. Barbiturates and codeine have no such effect.

Phillips (1945) tested the vestibular labyrinthine response to cold irritation in 64 cases. In a number there was delay and asymmetry of the responses. Eighteen of 24 cases which had no vertigo gave abnormal reactions. Vasomotor disorders resulting from the head injury are regarded as an important factor. Of 449 cases surveyed, 30 per cent. complained about giddiness.

Hooper, McGregor and Nathan (1946) observed the symptom of "explosive rage" which they relate to the "explosive diathesis" described by Kaplan in 1899. The patients were not as a rule irritable apart from the explosive attacks. From the forensic point of view these patients have to be regarded as insane at the time of the attack. Twelve cases are described. Four had been aggressive personalities before. In 3 cases there was a relationship to epilepsy. The prognosis is poor. One patient committed suicide.

Denny-Brown (1945) does not think that there is a relationship between acute traumatic psychosis following head injury and traumatic dementia.

Aita and Ristan (1948) studied psychotic reactions in the late recovery period following head injury. Among 500 cases evacuated to an army neurological centre several months after the injury, 4 cases of psychosis appeared which are described in detail. Two were schizophrenic reactions in which head injury played a secondary role. Two cases showed prolonged traumatic psychotic reactions of the confabulatory-amnesic type in which brain injury appeared to be the outstanding causative factor. Both were able to return to simple occupations despite intellectual impairment.

Kremer (1944) went through notes of 2,700 cases from a military hospital. Only 58 were considered to have personality changes. The invalids and the epileptics were excluded. Only 4 patients had committed offences following the injury. The author regards the increased proneness to neurotic reactions as the result of structural damage. Klingman (1945) also believes this often to be the case. He has found narco-analysis and narcotherapy useful in the treatment of these cases. Klingman describes the clinical picture of subdural haematoma or effusion. He observed the following syndromes: (a) retardation with flattening of emotional tone; (b) organic reaction type with restlessness; (c) psychosis precipitated by trauma; (d) post-traumatic psychopathy in the absence of previous psychopathic traits.

An indirect connection between traumatic and structural damage and neurotic symptoms is suggested by Rosenberg (1946) who gives a detailed report of a neurosis with obsessional features following head injury. The patient was given psycho-analytical treatment. The author describes how temporary cerebral impairment, by leading the patient into a personal relationship he could not maintain, may have played a significant part in the aetiology of the neurosis.

Thompson and McGinnis (1944) found that among the 61,795 cases admitted to the Los Angeles Psychopathic Hospital over a period of 17 years, 174, i.e. 0.28 per cent., were due to head injury. The ratio of males to females was 4 to 1. In order of frequency the following conditions were found; intellectual deterioration, personality disorder, post-traumatic delirium, other types (delusional and hallucinatory states, paranoid reactions).

Porter and Fetterman (1944) propose the following aspects to be considered in the differential diagnosis between psychogenic and physiogenic symptoms following head injury: (1) Pre-traumatic personality; (2) severity of the injury; (3) pre-traumatic alertness *versus* amnesia; (4) unconsciousness and delirium; (5) neurological signs; (6) localizing symptoms; (7) mental attitude and thought content in the later period; (8) material gain; (9) sequence of events. However, even with the help of this scheme the authors often find the distinction difficult to make.

Kant (1945) attempts a distinction between "somatogenic" and neurotic complaints. The former appear foreign to the personality and give an impression of genuineness, as opposed to psychogenic symptoms which have expressive value, appear non-genuine, changeable and influenced by suggestion. The patient with a somatogenic disorder tries to belittle his complaints while the

patient with a psychogenic disorder exaggerates his sufferings. The former is irritable in outbursts without apparent reference to his emotional situation, while the latter appears gradually to work himself up into a temper tantrum. When subjected to psychological tests the neurotic patient exaggerates and dramatizes his mistakes, which are sporadic, while the patient with organic impairment shows "genuine" fatiguability with a steady curve of decline. Kant's criteria are only of limited value as "somatogenic" and neurotic complaints often co-exist and modify each other.

Ruesch and Bowman (1945) studied 128 patients suffering from prolonged post-traumatic symptoms and compared them with acute head injuries, with brain disease and psychoneurosis. They conclude that in the late post-traumatic conditions the importance of brain damage has been widely overrated. While cases with severe brain lesions tend to improve as time goes on, post-traumatic conditions without neurological signs tend to get worse. Delayed recovery from head injury is conceived as the result of the impact of the trauma on abnormal character structure. Reactivation of infantile conflicts can commonly be observed. The same circumstances which may lead to accident seem to predispose to delayed recovery. The greatest incidence of delayed post-traumatic recovery was found in the middle class "with its tendency to conformance," while the lower class "with their tendency to overt misconduct" tend to accident proneness.

Ruesch, Harris and Bowman (1945) investigated the pre- and post-traumatic personality in their 128 cases. They evolved a maladjustment index based on such data as employment, marriage, alcoholism, childhood and adult environment, etc., and used a small number of simple psychological tests. They found the following permanent post-traumatic personality changes in a proportion of their cases; increased fatiguability, lowered tolerance to alcohol, unstable work record, decrease of interests and occasional impotency. They found overconcern with bodily functions and high hypochondriasis scores in the Multiphasic Inventory. Pre-existing neurotic tendencies seemed to prolong the duration of post-traumatic syndromes. The problem of accident proneness was also examined. All the results obtained seemed to indicate that the post-traumatic personality was more dependent on the pre-traumatic personality than on factors related to the accident.

Beck (1946) compared 172 patients with post-concussional encephalopathy due to blast or head injury, and 50 controls with functional anxiety reactions. Patients with focal defects were excluded from the first group. Abnormal eye signs (defects of convergence and accommodation, disturbed upward gaze, external muscle imbalance, blepharospasm, inequality of pupils, nystagmus) were the only neurological findings of differential value. One or more of them was present in 84 per cent. of the organic group and in only 20 per cent. of the controls. Under sodium amytal the post-concussional patients had a persistent amnesia for the period of injury, whereas the controls were able to reconstruct their entire experience.

Puech and Mallet (1946-47) investigated the remote consequences of head injury in 630 cases with the help of air studies and intracranial explorations.

They found gross organic lesions in 54 cases. They believe that psychiatric symptoms occur when the lesion is diffuse, and that a cortical and autonomic factor contribute in the genesis of many mental disturbances. The approach of the authors is purely organic.

Aita (1947) studied the late effects of injury to the brain by penetrating missiles in 100 cases. Prolonged amnesia was correlated with neurological symptoms. The resulting final disability could be comprehended only in the light of the patient's personality. It could not be accounted for merely on the basis of the severity and location of the injury as such.

There is common agreement on the need for systematic rehabilitation which should start as early as possible, as well as on the desirability of at least a psychotherapeutic attitude if not psychotherapy. Botterell and Wilson (1944) report on favourable results in 246 cases. According to Ritchie Russel and McArdle (1946), nine out of ten patients admitted to hospital with head injury make a quick and excellent recovery. Fettermann (1944) finds the prognosis best in young people with good personalities. Everts and Woodhall (1944) found that six out of every 100 battle casualties were head injuries, three-quarters of them closed. Their results with early progressive activities were highly satisfactory. Ritchie Russell (1949) recommends the establishment of a "head injury advice bureau" with a neurologist and a social worker, both with special experience in the rehabilitation of these cases. The author's advice bureau at Oxford, which began its activities three years ago, has been successful in preventing much chronic invalidism.

Murray and Halstead (1947) treated 88 soldiers with post-concussional syndrome by injections of afenil (calcium chloride urea) with good results. The favourable effect of this treatment confirmed the authors in their assumption that in the majority of cases the syndrome was due to vascular changes.

The frequency and the mechanism of post-traumatic headaches has been studied by several investigators. Guttmann's (1946) observations have already been mentioned. Brenner, Friedman, Merritt and Denny-Brown (1944) analysed their 200 cases in regard to occurrence and causation of post-traumatic headache, which was present at some time in 69 per cent. In 32 per cent. it continued longer than 2 months, in 20 per cent. it did not persist beyond the end of hospitalization, in 6 per cent. it set in only after discharge from hospital. Headache lasting for more than two months was associated with dizziness and new symptoms such as fear and irritability. Prolonged headache was frequent among neurotics and people with complicating environmental factors. Liability to provocation by histamine suggests localized vascular damage.

Ross and McNaughton (1944) compared 68 patients with persisting symptoms after head injury, with 22 observed after injury who had no symptoms. The greatest difference between the patients and the controls lay in the presence of situational factors which might have produced or aggravated neurotic symptoms. This was true for every type of headache. Patients with localized headache showed less evidence of previous neurotic background and more evidence of cerebral damage. Studies of the postural vascular responses did not indicate any effect in patients with head injury which differed from that in neurotics or in patients convalescing from other illnesses, nor have they given any lead

to treatment other than suggesting the value of exercises for hardening and relaxation.

Friedman and Brenner (1944) compared post-traumatic and histamine headache. Intravenous histamine injection produced in 13 out of 22 cases a headache identical in localization and character with the headache from which each patient had suffered after head injury. Headache appeared as the blood pressure was rising. Histamine injection seems to activate some types of post-traumatic headaches. In 3 cases marked improvement followed the injection.

Simons and Wolff (1946) found post-traumatic headaches in only slightly more than half their cases of head injury. They describe three types of chronic headache: (1) Sensation of pressure or aching pain of cap-like distribution, or with localization to a circumscribed area other than that of the injury; (2) similar to the above, but with localized tenderness over the site of the impact; (3) attacks of aching, throbbing pain. Electromyographic studies have shown that Type 1 is associated with abnormal electrical activities of the muscles of the scalp and upper part of the neck. This type of headache can be relieved if the muscles are infiltrated with novocaine until the electrical activities disappear. Type 3 is of vascular origin and may be relieved by injection of ergotamine tartrate. It is similar to that following histamine injection.

Wolff (1948), in his book on headaches and other head pain, points out that the sustained contractions of the muscles of head and neck which are supposed to be responsible for the most frequent type of post-traumatic headache, are as a rule associated with sustained resentment, anxiety, frustration, tension and fear. The amount of muscular control is minimal.

Watts, Wiley and Groh (1945) reported on observations which indicated that post-traumatic headaches were in some cases related to the scalp arteries.

Blast injuries.—Anderson (1942) described psychiatric syndromes following blast. He observed 8 cases showing a variety of symptoms with organic features. In view of the absence of head injury and often of unconsciousness, these symptoms are usually overlooked. Although the possibility of head injury could not be excluded, none of the cases showed retrograde amnesia. Possibly in some cases the central nervous system is affected without other structures suffering damage. Slight intellectual impairment was present in at least 6 cases. Memory for the event was imperfect, and in some cases there was a global amnesia. Consciousness was clouded immediately after the explosion. Two types of emotional changes were found; affective lability and apathy, the latter being more frequent. There was a general slowing down of motor activities. The author points to the medico-legal significance of these states. An offence might be committed during one of these clouded periods of which the patient has no subsequent memory.

Aita and Kerman (1946) studied 34 cases which had been exposed to blast. Two-thirds had been unconscious. Headaches, tinnitus, deafness, dizziness, faintness, backache and anxiety symptoms occurred regularly. The Minnesota Multiphasic Personality Test showed a high incidence of hypochondriasis,

depression and hysteria scores. Forty-eight per cent. of the 34 cases were regarded as incapacitated for further Army service. They showed a high incidence of confusion, amnesia, "organic" performance on psychological tests, regressive changes in their behaviour and E.E.G. abnormalities. Violence of trauma, degree of organic changes and severity of residual disablement were not directly related to each other. Those considered incapacitated for further service had in their histories previous combat experiences, propensity to invalidism, and had been subjected to prolonged hospitalization.

Schwab (1947) examined 350 cases with blast concussions admitted to Naval hospitals. Over 90 per cent. had hysterical anxiety states. Forty per cent. complained of periods of amnesia lasting from 30 seconds to 30 hours. This led many clinicians to the conclusion that there must be cerebral damage, but there was no retrograde amnesia in any of the cases. The amnesia usually reported began when the subject had heard the explosion and felt himself pushed away by it. Narco-analysis and hypnosis restored the amnesia and revealed violent fear reactions and surrender to the flight impulse.

Hamlin, Denny-Brown, Schwab and White (1948), in a discussion of the neurological effects of blast injuries agreed that the psychological effects were more important than the neurological ones.

Head injuries in children.—Guttmann and Horder (1943) investigated the after-effects of head injury in 60 children (under 15 years of age). Boys were more numerous than girls. Two-thirds of the cases were due to road accidents. The intelligence of the children was average. Fractures of the skull were more frequent than among adults. In the acute stage emotional symptoms were more impressive than clouded consciousness and intellectual loss. The incidence of headaches was about the same as in adults. Two-thirds of the cases were fit for discharge after two weeks in hospital. Absence from school due to accidents was two to seven weeks in half of the cases, in one-quarter less and in one-quarter more. The post-concussional syndrome was observed in 10 per cent. of the cases; its incidence depended largely on environmental factors. Irritability was the most common after-effect. In one case there was definite deterioration in school performance, but this was a child with traumatic epilepsy. Only in 2 cases was there an indication of personality change.

Fabian and Bender (1947) made an inquiry into predisposing factors in 86 children with head injury admitted to the Bellevue Hospital, New York. The highest number was in the five to six age range, as also in other accidents. Ninety-two per cent. of the children were boys. In 25 per cent. special factors could be found (mental defect, epilepsy, organic brain disease, psychosis). Forty-two cases had had previous accidents; 17 of them had had at least two major head injuries previously. Mental abnormality among the parents was found among 83 per cent. of the cases. The home atmosphere in these cases was one of hate, rejection and violence. Accident habit in children was over-determined, but the bad child-parent relationship was most important. Strong sado-masochistic patterns were found in the personality profiles of the accident-prone group. Identification with a sadistic father was marked in boys. In some cases an active Oedipus conflict was significant.

Psychometric Tests.—Reynell (1944) reported the results of psychometric tests in 1,500 cases of head injury. He found them a valuable pointer in prognosis. Cases showing intellectual loss two months after injury carry a worse prognosis. While nine out of ten cases with personality changes showed evidence of intellectual loss, the reverse was not true. The most constant finding was a falling off in performance, especially when tested with Kohs' blocks. Eighty per cent. of head injuries will show no intellectual impairment.

Ruesch and Moore (1943) investigated intellectual functions in the acute stage of head injury. One hundred and ninety patients were subjected to a series of psychological tests within 24 hours following the injury. There were three stages in the recovery of intellectual functions during this period; complete failure, failure of serial subtraction alone and impaired performance in several tests. Serial subtraction was found to be the most sensitive test.

Moore and Ruesch (1944) found that all patients with intellectual defect persisting after 6 months following the injury had had a post-traumatic amnesia of at least 19 days.

Ruesch (1944) studied the frequency and nature of intellectual impairment in head injury. Mental functions affected were primarily: speed, judgment, ability to keep up a sustained effort. Half of all subjects suffering from head injury show slight intellectual defects which decrease gradually, usually within three months. The impairment was related to the severity of the injury.

Linn, Levine and Hewson (1945) report on the use of psychological tests for the clinical evaluation of late diffuse organic, neurotic and normal reactions after closed head injury. They evolved a three-hour battery with the help of which they were able to differentiate the relative participation of diffuse organic and chronic neurotic factors involved in mental and personality deviations. Cole (1945) assessing intellectual deficit in head injury is of the opinion that head injury is less of a problem to the patient who is intellectually well endowed. He questions the specificity of traumatic intellectual deficit, but believes that the prognosis of a given case can be estimated with the help of tests.

Zangwill (1945) reviewed the psychological work at the Brain Injury Unit, Edinburgh. He gives an account of the scope and limitations of the clinical psychologist working in such a unit. He refers to the studies carried out by him, some jointly with Paterson; some of their publications have been reviewed earlier in this survey.

Zangwill (1947), in another contribution, discusses the psychological aspects of rehabilitation. The clinical psychologist is mainly concerned with the convalescent patient. It falls to him to develop adequate methods of assessing the various types and grades of disability. He is called upon to decide whether re-education on the psychological level is practicable, and if so, how it is best carried out; how far the patient can be expected to compensate for his disability, and to what extent the brain is capable of re-education. The most important contribution of the psychologist lies in the proper assessment of residual disability. Here psychometric tests have to be used with caution.

Tooth (1947) reported on the use of mental tests for the measurement of disability after head injury. He compares the results of differential testing in patients with head injury and in psychoneurotics. Among the former, those

judged to be most severely injured on clinical grounds gave the most specific type of test pattern. This is interpreted as evidence that the method is testing some factor associated with failure to recover after head injury. However, the deviation of individuals may be so slight and so variable that the method is of limited value in the assessment of the individual case. As neurotic subjects showed a pattern of differential failure similar to that found in patients with head injury, this failure could not be regarded as peculiar to the organic impairment. The test results of hysterics most nearly matched those given by the patients with head injury.

Allen (1947, 1948, 1949) compared the test performances of patients after head injuries with those suffering from brain disease. The results indicate that the functioning and efficiency of both groups follow a similar pattern. Those with brain injury tend to show more marked discrepancy between verbal and performance subtests. The author holds that the statistical findings do not fully justify the quantitative interpretation. Chance factors played too important a role. An unmeasurable consideration must be given to the impact of the injury and disease upon the personality of the patient.

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NEURO-SYPHILIS AND ITS TREATMENT.

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SINCE the last review of literature was published in this Journal, penicillin has been added to the armamentarium of chemo-therapeutic agents for the control not only of early syphilis, but of those later manifestations of the disease many of which are the direct concern of the neuropsychiatrist. Penicillin has, in fact, dominated the literature during the last five years and it is the purpose of this article to sift the vast accumulation of papers and make some attempt to present the more important work which may be of interest and assistance to the worker in the field of neuropsychiatry.

ASYMPTOMATIC NEUROSYPHILIS.

The need for early diagnosis cannot be too often stressed when the application of some prophylactic measure will prevent the later onset of symptoms. As the disease progresses, the more definite entity of symptomatic neurosyphilis, including the still later manifestations of general paralysis, tabes, or both (taboparesis), and occasionally the presence of optic atrophy become manifest.

The term "asymptomatic neurosyphilis" implies a disease process which can only be detected by the presence of abnormalities in the cerebrospinal fluid due to syphilis, unaccompanied by any clinical signs or symptoms. So important is the recognition of this that it is well to recall the classification of the types of abnormality of spinal fluid as advocated by Earle Moore and other workers in America. Group I fluid reveals a slight increase of cells 5-30, with normal protein content, a negative colloidal gold curve and a negative Wassermann. In Group II the cells are similarly increased as in Group I, protein may be raised from 30 to 70 mgm. per cent., the changes in the colloidal gold curve are variable and Wassermann weakly positive, while in Group III the cells are increased from 10 to 200, protein from 50 to 200 mgm. per cent., the Wassermann is strongly positive and the colloidal curve exhibits what is recognized as the paretic formula, the first five tubes being completely decolorized.

Hahn and Clark (1946), in an analysis of 1,800 patients treated at the Johns Hopkins Clinic between the years 1914 and 1941, provide a useful analysis more especially with regard to the prognosis of neuro-syphilis. Out of these 1,800 patients were selected 533 with at least two cerebrospinal fluid examinations, and 467 with at least two physical examinations. These authors make a sharp distinction between early and late asymptomatic neurosyphilis; the early type includes those patients with a definite history of two years or less from the primary attack, while in the later form the interval of time between the original infection and the discovery of fluid abnormality is more than two years. It is clearly brought out that the ultimate prognosis is very dependent on the

type of fluid abnormality and the duration of infection. In other words, the more strongly positive the initial fluid examination, the more unfavourable is the prognosis with respect to the final cerebrospinal fluid outcome, and the longer the duration of syphilis the more strongly positive and more resistant is the fluid to treatment. The probability of developing clinical neurosyphilis by the fifth year of observation was 16.2 per cent. in patients whose fluid became worse or remained unchanged, as contrasted with only 3.1 per cent. in patients whose fluid became negative or significantly improved. By the tenth year of observation these probabilities were 33.2 per cent. and 6.8 per cent. respectively. The risk of developing parenchymatous neurosyphilis increases directly in proportion to the severity of the initial cerebrospinal fluid involvement. It was difficult to assess the relative merits of different types of treatment, as supplementary treatments, tryparsamide or malaria, were applied only to those patients with more resistant fluids. The relatively benign nature of many positive fluids was demonstrated by the fact that 3 of 12 untreated patients and 46.3 per cent. of 218 "totally inadequately" treated patients ultimately attained a negative fluid. It would appear, therefore, that the prognosis in many patients with asymptomatic neurosyphilis is favourable even when treatment is "totally inadequate"; in fact the probability of clinical progression over a ten-year period in untreated asymptomatic neurosyphilis was estimated at approximately 20 per cent. Adequate routine treatment alone was sufficient in many cases; there was no evidence that tryparsamide as an adjunct to routine chemotherapy was of any value. Malaria was given to 40 patients, one half of whom had Group III fluids, and who had proved resistant to other forms of treatment. Negative fluids were obtained in 25 per cent. of cases and in no case did the fluid abnormality progress; clinical progression even in this resistant group was 9.5 per cent. at the end of five years' follow up, with no increase at the end of ten years.

Merritt (1945) found that asymptomatic neurosyphilis was present in 9.5 per cent. of 2,263 patients with syphilis; of 676 cases of neurosyphilis of all types, asymptomatic neurosyphilis constituted 32 per cent. of the total. "The medical profession has the means of preventing symptomatic neurosyphilis, and it is criminally negligent if it does not avail itself of them." In a more detailed analysis of 200 patients, 110 males, 90 females, the sex incidence was relatively equal, which is in sharp contrast to that found in parenchymatous involvement, where the male is a much more frequent victim. Three-quarters of the patients had Group I fluids, none of whom developed any form of parenchymatous neurosyphilis and only 4 per cent. showed signs of symptomatic neurosyphilis of the meningovascular type; on the other hand, 20 per cent. of patients with Group III fluids developed parenchymatous neurosyphilis. This author employed routine treatment with trivalent arsenicals and bismuth in the first place. If complete reversal of fluid is not obtained in 18 to 24 months, or in whom after 30 or more injections of trivalent arsenic examination of the fluid reveals marked abnormalities, then immediate recourse to tryparsamide or some form of fever therapy, is recommended.

Scherlis and Caravati (1946) give a review of the incidence of neurosyphilis in younger age groups. In their study of 128 Army cases, 90.7 per cent. were

between the ages of 20 and 40 ; one patient was under 20 and one older than 50. Routine examination of cerebrospinal fluid showed the presence of neurosyphilis in 108 (84 per cent. of cases), while in only 20 cases (15.6 per cent.) was diagnosis established following investigation of some specific complaint. Of this group investigated 53 (41.4 per cent.) were cases of asymptomatic neurosyphilis, 8 with Group I fluid abnormality, 15 with Group II and 30 with Group III.

SEROLOGICAL FOLLOW UP.

Not only is the interpretation of a fluid examination of primary diagnostic importance, but the need for repeated examinations after treatment, in order to check the arrest of the disease process, is equally necessary. Carl Lange and Harris (1945) discuss the important implications of the paretic formula and the need for its quantitative differentiation. They raise the question of the effect of efficient therapy depending on the ratio between the degree of inflammation and degeneration present. While the number of cells in the cerebrospinal fluid reflects a quantitative expression of the inflammation in the meninges and perivascular spaces, of equal significance is the increase of total protein, which is the result of lysis of dead cells. In fact the early effect of therapy often produces a fleeting increase in the protein content. These authors refer to the poor prognostic significance of those cases of general paralysis with a very low or even normal cell count, which indicates a torpid inflammation and an unsatisfactory defence mechanism, especially if accompanied by signs of advanced degeneration.

Dattner, in his excellent monograph on *Neurosyphilis* (1944), leaves no doubt on the paramount importance of a serological follow up. Only recently (1948) he reiterates the need for a complete examination, and he refers to the four investigations, the Wassermann reaction, cell count, protein content and colloidal gold test as obligatory. To quote his conclusions, he says :

"They form a syndrome which must be interpreted as a whole. No single item will give complete information on the process involving the central nervous system. The cell count indicates activity of the process : the total protein in association with the cell count may indicate activity : the colloidal gold test in its qualitative aspect gives a clue to the prevalent type of central nervous tissue involvement, and its quantitative values offer a revelation of the trend of the process ; and finally, the complement fixation test signifies the specific nature of the disease, and the quantitative reagin readings, together with the other tests, inform us if the syphilitic process in the central nervous system is progressing, abating or has been definitely checked."

From the Horton Hospital Malaria Therapy Centre, Whelen (1946) reported a detailed analysis of the serological follow up of over 500 cases. She adopted the classification of results, as enunciated by Dattner, Thomas and Wexler (1944), who refer to strongly positive, weakly positive, inactive and negative fluids. The strongly positive fluid corresponds to the Group III fluid of Earle Moore's classification ; in the weakly positive fluid the Wassermann may vary from strongly positive to positive, the cell count may be normal or slightly raised, the protein is increased and the Lange curve remains paretic. The inactive fluid is of importance, in that the Wassermann is positive, but cells

are normal, protein is markedly reduced and the Lange may or may not be paretic; the negative fluid is a normal fluid in every respect. All the cases investigated by Whelen were cases of general paralysis or taboparesis; the longest time between treatment and the last examination was 15 years and the shortest one year, the average for the total being 2 years. While a persistently positive fluid is indicative of the need for further treatment, it was of interest that in many cases when once an "inactive" fluid is obtained, this state of affairs remains stationary. The significance of this inactive fluid was carefully analysed and of 529 patients (347 men, 182 women) it was found that, of the men, 24 (7 per cent.) eventually relapsed, the fluid becoming strongly positive; in 10 it reverted to a weak positive, in 199 (57.3 per cent.) it eventually became negative, and in 114 (32.8 per cent.) it remained inactive. The analysis of the women gave fairly similar results. Generally speaking, at the end of the first year the condition of the fluid was a fairly reliable indicator as to whether further treatment was necessary or not. A further point of immense practical importance was the discovery that in over 90 per cent. of patients showing two consecutive "negatives" at an interval of six months or more, the spinal fluid remained persistently negative. The realization of this fact is of value to both patient and doctor, with the obvious conclusion that no further treatment is necessary.

The inclusion at this point, of serological findings relating to malaria therapy for general paralysis, at the other end of the scale from the problem of asymptomatic neurosyphilis, might appear out of place, but it illustrates only too well the need for serial lumbar punctures in all cases of neurosyphilis, whether symptomatic or not, in evaluating the progress or arrest of the disease.

The education of the patient to the need for follow-up tests is necessary; not only for the patient, who is at work, but for the hospital authorities where beds are at a premium, so that investigations in out-patients are of great assistance. Complications following lumbar puncture should be reduced to a minimum. Underwood (1946) presented a statistical analysis of 500 punctures. He quotes the findings of several workers and reports the incidence of post-lumbar-puncture headache, varying within wide limits ranging from 1 to 40 per cent. among patients so investigated. These differing reports are difficult to explain, as also is the report that cisternal puncture (Kulchar) reduces the frequency of headaches. The use of pituitary extract (1 c.c.) by Solomon relieved many patients. Guttman found complete relief with ergotamine tartrate in 29 out of 35 patients. Underwood, using a 22-gauge needle and 2 c.c. of 2 per cent. novocaine locally, collecting 6 to 8 c.c. fluid, found incapacitating headaches in 19 per cent. of cases; rest in bed after the spinal puncture did not reduce the incidence of post-lumbar puncture headache. At the Horton Hospital Clinic, where the Dattner needle with Harrison's modification (Down Bros.) has been employed for over 10 years, headaches have only rarely been encountered. This is largely attributed to the practice of allowing patients to leave the out-patient clinic almost immediately and not encouraging them to lie down afterwards. Levin (U.S. Army Medical Department) confirms this: by keeping patients active only 15 patients (0.67 per cent.) reported severe headaches in a series of 2,237 lumbar punctures; he suggested that intra-

cranial hypotension and lowered spinal pressure are overcome by moderate exercise, thus preventing a compensatory oversecretion of fluid and hypertension with resultant headache.

PENICILLIN.

It is only possible to refer to the more important papers dealing with this complicated problem. The literature is so extensive that it is difficult to steer a steady course and present conclusions which are of useful application to the clinician. For more detailed analysis and for a far better presentation than is possible in this paper, the reader is advised to refer to an excellent monograph by Earle Moore, *Penicillin in Syphilis* (1947), with an extensive bibliography up to 1946.

THE ACTION OF PENICILLIN : ITS PHARMACOLOGY AND EXPERIMENTAL WORK.

Much experimental work on animals has been carried out. The work has been chiefly done with rabbits. Frazier and Frieden (1946) review the available evidence and the theories put forward as to the action of penicillin on the spirochaete. Experiments *in vivo* are reported by Dunham and Rake, who advance the theory that penicillin probably destroys the reproductive capacity of the spirochaete without destroying its power of motility. Frazier and Frieden themselves found changes in the morphology of spirochaetes as the result of penicillin therapy. The length of the spirochaete altered considerably, there being an increase in long forms (14 to 22 microns) ; these long forms were less motile than the short forms, an indication in their opinion of excessive growth of the organism eventually causing its death.

Eagle, Magnuson and Fleischman have contributed many studies in elucidating both the pharmacology and possible clinical applications as afforded by their experimental investigations. They found that the effect of hyperpyrexia improved the therapeutic efficacy of penicillin in experimental syphilis (1947). By employing a "fever box" for rabbits with temperatures up between 104° F. and 106° F. for ten hours, the therapeutic efficacy of penicillin was increased at least eight- to ten-fold if penicillin and fever were simultaneously administered. With penicillin alone, 64,000 units per kilo body weight was required to cure 90 per cent. of animals, compared with 8,000 units per kilo weight, the latter dose being combined with fever.

The preparations of penicillin in general use are mixtures of the sodium salt and varying amounts of other substances, the nature of which is not known. From pharmacological studies in various clinics—Arnold, Boak and others (1947), Turner and others (1947), to quote only two more recent papers—it has been established that in experimental syphilis, penicillin G is superior in spirochaetocidal effect to F, K and X ; F requires six times as large a dose as G to achieve the same effect. Turner and his co-workers ask why it is that a relatively small amount of penicillin will kill well over 90 per cent. of *Treponema pallidum* in the skin syphilomas of experimentally infected rabbits, leaving a relatively small proportion of organisms which appear disproportionately resistant to destruction by penicillin.

PENICILLIN: DOSAGE AND METHODS OF ADMINISTRATION.

Further experimental studies by Eagle, Magnuson and Fleischman (1946) throw light on the various possibilities of obtaining the maximum therapeutic efficacy. Even if the problem is limited to the action of commercial penicillin injected intramuscularly in aqueous solution there are three variables; the number of injections, their frequency and the total amount of the drug administered. In rabbit syphilis it was found that the curative dose was affected to a marked degree by the number of injections—the greater the number, the less was the total amount of penicillin required for cure. Also, provided the interval between the injections was long enough to avoid cumulative effect on the blood penicillin level (in which case therapeutic efficacy was paradoxically decreased), it made no difference whether penicillin was given 4-hourly, twice daily or daily; an equal number of injections at a given dosage level produced the same effect. Their findings are important from the point of view of clinical application: (1) Relatively low tissue concentrations of penicillin acting over a long period of time (the pattern produced by many small injections) were regularly more effective than high concentrations maintained for a short period (the pattern obtained with a few large injections). (2) High peaks of concentration represent waste of penicillin; it is better to prolong the total duration of treatment instead. (3) Although a minimum interval must be allowed to permit each dose to exercise its maximum effect, this minimum interval is not necessarily the optimum. From experimental data the interval can be prolonged far beyond the minimum without affecting the therapeutic efficiency. This last consideration raises an important application regarding the possibility of giving treatment on an ambulatory basis. In this country Lloyd Jones (1946) obtained good results in the treatment of primary and secondary syphilis with intramuscular injections (300,000 units) once daily. Laurie (1945) and others similarly advocate the ambulatory treatment of early syphilis on experimental evidence; they recommend three doses of 600,000 units at hourly intervals given on five successive days. A more important modification suggested by many workers is the preparation of calcium penicillin in oil and beeswax. Eagle and his co-workers (1947) found in their experimental work that treatment with the oil-beeswax preparation was from 2 to 14 times more effective than the aqueous solution in producing a cure. This superiority, however, was less noticeable in longer treatment schedules, the margin of difference between the two preparations became less as the number of injections was increased, and the amount per injection was decreased. The question of wastage was again emphasized in that high blood levels with large amounts of the aqueous solution contribute little to therapeutic efficiency. All the experimental work so far under review refers to the treatment of early syphilis.

As far as the problems of neurosyphilis are concerned, there is considerable divergence of practice not only in the method of administration, but in the amount of penicillin used. How far can this be assessed in the light of experimental work? Reynolds and Moore (1946) in their review of recent literature quote Raiziss' experiments in rabbit syphilis, where infections were cured by 40,000 units of penicillin per kilogram body weight over a period of 8 days.

On this basis for a human adult of 60 kg. weight, the dose required would be 2.4 mega units. In the early trials of penicillin in neurosyphilis the amount recommended was in the region of 2 mega units, but it was found that more rapid healing was obtained in Raiziss' work with double the dose, i.e. 4.8 mega units. Rose and Solomon (1947), however, after clinical trials recommended an increase to 6 mega units; they found that with 3 mega units even when combined with fever therapy it was necessary to re-treat more than one-third of their cases after one year's observation. Another vexed problem which has been the concern of many workers is the question as to how far it is necessary, if indeed possible, to obtain a high concentration of penicillin in the cerebrospinal fluid. Weickhardt (1946) tried intrathecal administration of penicillin in cases of general paralysis; though the number of patients for whom this method was used was only five, one of whom died, he regarded the method as safe, but in an experimental stage. The reports of authorities quoted, however, as having tried similar methods, were far from encouraging. McDermott and Nelson (1945) question the need for a high concentration of any chemotherapeutic agent in the cerebrospinal fluid of a patient being treated for neurosyphilis. These workers employing dilution techniques of bio-assay found no penicillin demonstrable in the spinal fluid of 70 patients treated for neurosyphilis. On the assumption that in neurosyphilis, even when meningitis is present, the rate of infection is relatively slow, the continued presence of minute amounts is probably all that is necessary for effective therapy following parenteral administration. This is in contrast to the treatment of the most acute purulent form of meningitis, where such method of administration might prove dangerously inadequate.

The beeswax-peanut-oil preparation of penicillin may well prove to be the method of choice in administration. Kirby and others (1945) studied the absorption and excretion of penicillin following 359 intramuscular and subcutaneous injections of a commercially prepared penicillin-beeswax-peanut oil mixture containing 4.8 per cent. beeswax and 300,000 units of penicillin per c.c. With intramuscular injections there was wide variability of absorption and excretion; in most cases the measurable level of penicillin was sustained for only twelve hours, which is not so good as penicillin assayable levels maintained almost continuously by injections every three hours round the clock. But is this continuous maintenance level really necessary in the therapy of neurosyphilis? These workers reported, however, that measurable concentrations of penicillin were prolonged more constantly with subcutaneous injections than with intramuscular. The authors consider the method safe, though many have complained of difficulty with syringes and the thick suspension of the preparation.

Dowling and others (1947) undertook a detailed investigation of various preparations and they record many advances in the manufacturing process. Fluid preparations of penicillin in oil and wax are now available and are preferable to the more viscid ("solid") ones, which require heating before injection. The liquid preparation, using crystalline penicillin, will produce as much prolongation of blood penicillin concentrations as the amorphous viscid preparations. In the investigation it was found that the size of the particles of peni-

cillin used in preparing the liquid forms influenced considerably the prolongation of the blood penicillin levels. A method was devised for determining the weight of the penicillin particles—"large particle" preparations measuring more than 50 microns and containing 50 per cent or more of the total relative weight were classified as such and those preparations with less than 50 per cent. of the particle by relative weight were classified as "small particle." Preparations containing crystalline penicillin can be stored at room temperature for eighteen months. The authors conclude that for ease of administration as well as the concentrations of penicillin achieved in the blood, the liquid preparations of crystalline penicillin of large particle size are the most satisfactory form of penicillin in oil and wax.

CLINICAL RESULTS OF PENICILLIN THERAPY.

We are fortunate in having access to trials of penicillin alone from many sources. In the past so many papers have led to confusion in assessing the relative merits of one or other new therapeutic agent, on account of the patient having received other forms of therapy either before or after or concurrently with the trials under review. Results may be grouped under two headings—clinical and serological.

Clinically there is general agreement that patients gain weight and feel quite different in themselves. This refers more especially to those more advanced forms of symptomatic neurosyphilis, general paresis, taboparesis and tabes. Heyman (1947) refers to cases of early paresis in which the response to penicillin was often quite dramatic, with immediate improvement of tremors, handwriting and slurring of speech. He reports also subjective improvement in cases of asymptomatic neurosyphilis, who describe themselves as "one hundred per cent. different"; many obtained relief from headaches, malaise and muscular aching. Nicol and Whelen (1947) report similar clinical improvement, particularly in patients who were confused and in poor physical condition, often observed during the actual course of penicillin, a phenomenon rarely encountered during malaria therapy. Gammon *et al.* (1946) refer, too, to the sense of well-being experienced by paretics after penicillin; they also report considerable amelioration in 82 per cent. of 40 tabetics, in whom lightning pains were a serious feature. The improvement in the tabetic is difficult of assessment due to the large subjective element. Koteen (1947) and his colleagues report improvement of lightning pains in 17 out of 24 patients and also of ataxia in half the series; gastric crises failed to respond.

Serologically there is general agreement by all authorities that penicillin produces profound and uniform effects in the cerebro-spinal fluid, regardless of the clinical syndrome treated. In asymptomatic syphilis, meningovascular neurosyphilis, general paresis and tabes, the cell count and protein content are reduced to normal limits in practically all cases.

While these reports are encouraging and lead some observers to the conclusion that penicillin may well replace malaria, it must be recorded that they are provisional and a word of caution must be added. In fact, O'Leary, Brunsting and Ockerly (1946) are unconvincing regarding the use of penicillin, they are doubtful as to penicillin being capable of controlling parenchymatous forms

of neurosyphilis, but favour its use in the treatment of the asymptomatic type. Gammon and Stokes (1946) suggest penicillin as the first choice for treatment of neurosyphilis, but qualify this statement for treatment of severe paretics. They used penicillin alone in 161 cases of neurosyphilis, using doses ranging from 1.2 to 2.4 mega units; this regimen was increased later to 4.8 mega units, either in a single course in 8 days, or two courses of 2.4 mega units in 8 days at 7 month intervals, or a single course in 16 days. Most workers give penicillin in repeated doses throughout 24 hours. Koteen (1947) and his co-workers use 300,000 units daily (in 25,000 units doses) over a two week period and conclude that an increase of the daily total dosage would not increase the effectiveness of therapy. Nicol and Whelen at the Horton Centre have been using 300,000 units daily in one dose for 14 days, but recently this routine has been changed to 300,000 units twice a day.

There is much to be said in favour of injections once or twice daily, in place of repeated injections every four hours, not only from the point of view of the patient, but of a depleted staff as well. Heyman (1947), in a preliminary observation found that the use of 4 to 6 mega units will probably arrest a neurosyphilitic process in 85 per cent. of cases. He adds a word of caution, however, and the need for more prolonged observation; patients with maximal fluid changes and the later severe types of neurosyphilis did not respond so well as those with less severe fluid findings.

Dattner (1947) is of the opinion that so far penicillin, when given in adequate doses, is at least as effective in the treatment of neurosyphilis as combined fever and antispecific therapies. He qualifies this statement by adding that we are ignorant of "the optimal relationship of dose and time to obtain the maximal therapeutic success." In this country, Purdon Martin (1948), with a series of 24 cases, including various types, studied at the National Hospital, Queen Square, started with 2 mega units, but eventually increased the dosage to 5 mega units. He stressed the need for patience and allowing time to elapse before a second course of penicillin is embarked on or some other therapeutic course adopted. Stokes and Steiger, with others (1946), give a useful analysis of the follow up of 283 patients with neurosyphilis; these workers report that the maximum improvement in serological reactions is evident within 120 days of termination of a course. They also raise the important question of possible wastage of penicillin; with a low dosage ranging between 1.2 to 4.8 mega units and a high dosage (4.8 to 10 mega units) they find surprisingly little difference in therapeutic effect, though there may be a slight trend towards superiority with the higher dosage. The same group of workers have published a further report (1948) in which some of their original clinical material is followed up. They find a tendency for marked serological improvement to level off at around 70 per cent. of all cases by the second year. At the end of two years serological improvement in different clinical types is expressed in percentages in the accompanying table:

	General paresis.	Tabo- paresis.	Tabes.	Asymptomatic neurosyphilis.
Reduced fluid	61	61	75	77
Normal and near normal	33	40	55	61

Only 14 of 317 spinal fluids became worse. It would appear from their analysis that serological improvement increases steadily up to the end of two years, after which there is no significant difference, when the fluids are checked up at the end of the third year.

Marked symptomatic improvement was observed in 46 per cent. of paretics, 35 per cent. of taboparetics, 33 per cent. of tabes and 47 per cent. of meningo-vascular syphilis; with the exception of tabes the clinical improvement in the other three categories was definitely greater at the end of the second year. The total improvement remained much the same, but evidently penicillin, like malaria, has a long period of cumulative improvement after the termination of treatment.

There is still very little to choose between the higher and lower dosage régimes, nor is there any real evidence that additional courses of penicillin produce better results. This again is in accord with experience of malaria therapy.

This group have now adopted for symptomatic neurosyphilis a single course of 9.6 mega units over 10 to 15 days, using a two-hour interval instead of a three-hour interval between round-the-clock injections. While they admit that some of the penicillin will be wasted, they hope to reduce the number of relapses still further and increase the rapidity of achievement of maximum effect.

In a review of 91 cases of asymptomatic neurosyphilis, 48 of early type and 43 late, Earle Moore and Mohr (1946) report favourably (only 4 patients had a serological relapse within the limits of a six months' to one year's follow up); none in the early group developed any clinical evidence of neurosyphilis. Of those in the late group no patient developed symptoms, though in one unequal pupils were recorded. These authors, in light of the classification of fluid abnormalities into Groups I, II and III, admit that in the first two groups abnormalities in some cases may disappear spontaneously, though a high proportion in Group II, if untreated, will eventually develop symptomatic neurosyphilis. Group III abnormalities seldom, if ever, disappear spontaneously; on the contrary, most of this group develop symptomatic neurosyphilis if untreated and many progress to the stage of the parenchymatous type of disease. Moore and Mohr recommend for the early type of the asymptomatic form not less than 2 to 4 mega units for patients with Group I and II fluids; for Group III fluid, 6-10 mega units should be given (120-200 intramuscular injections of 50,000 units every 3 hours, day and night, for 15 to 25 days). In late asymptomatic neurosyphilis for Group II fluid, not less than 4 mega units over 10 days; while in Group III fluid the same regimen as for the early type is recommended, with the proviso that fever therapy might be a necessary adjunct. It would appear, then, that the dosage required for the more serious types of symptomatic neurosyphilis is definitely within the range of 6 to 10 mega units. These workers wisely sound a note of warning and state that a minimum of five years' study and the treatment of many more patients will be required before we can arrive at any definite conclusions.

THERAPEUTIC REACTIONS IN PENICILLIN THERAPY.

While there is much evidence that toxic reactions in patients treated for primary or early syphilis by penicillin are relatively common, the incidence of similar reactions occurring during penicillin therapy for neurosyphilis seems to be much lower.

Morginson (1946) gives a formidable list of protean reactions, including severe skin lesions, headaches, vertigo, dyspnoea, the precipitation of latent epilepsy and in some cases mental reactions exhibiting euphoria, depression or confusion. He quotes experimental evidence and clinical observation indicating that commercial penicillin and crystalline penicillin both possess definite antigenic and allergenic properties. Another theory put forward is that the toxic action of penicillin depends on impurities resulting from the manufacturing process.

Peck and his co-workers (1948) in a recent communication give an extensive review on the clinical problems of penicillin sensitivity. Their investigations deal chiefly with allergic eruptions and their experiences with penicillin desensitization. In their opinion the most important test of penicillin sensitivity is the delayed reaction to the intradermal injection of penicillin, readings being recorded 48 hours later, the reaction being similar to that of a trichophyton test. They find that there are two relatively common types of reaction to treatment with penicillin: type 1, an urticarial, serum-like type in which sensitization is induced by treatment; type 2, reactions of an erythematous-vesicular eruption, resembling the trichophytids. In type 1 urticaria and the erythemas, together with joint pains and fever in some cases, occurring after a definite incubation period, are the commonest allergic reactions seen. In some cases the eruption is limited to the buttocks and thighs, while in others the distribution is general but in the majority there were none of the accompanying manifestations of serum sickness. Occasionally it manifests itself several days after treatment with the drug is completed; the usual incubation period, however, was 7 to 12 days. Of particular interest was the preponderance of men who gave a positive reaction to a cutaneous test with penicillin after 48 hours. In type 2 sensitivity is present in a latent or an active stage. In the latent stage there is no clinical phenomenon, but simply a positive cutaneous reaction at the end of 48 hours without a history of previous penicillin administration; this reaction is the so-called spontaneous one of the tuberculin type. The active stage manifests itself with a characteristic erythematopapulo-vesicular eruption, which, though sometimes generalized, is most severe on the hands and feet and in the groins, the bullous reactions becoming pustular; pruritus may be severe. The localization to the hands and feet is suggestive of a relation between these symptoms and previous fungous disease of the skin. Again the incidence was more common in men than in women.

These authors recommend the need for cutaneous tests on all patients for whom penicillin treatment is recommended; parenteral and oral methods of desensitization are described. Investigations were carried out on 406 adults and 93 children, who were tested with penicillin and trichophytin. Of 276 adults who had never had penicillin, 15 or 5.4 per cent. reacted "spontaneously" to the penicillin cutaneous tests. Of 168 men, 11, or 6.5 per cent. reacted

positively; of 108 women 4, or 3.7 per cent. were positive; no positive reaction was recorded in the children. Immediate intradermal cutaneous tests, in which wheals were looked for after 10 to 15 minutes, were negative in all patients tested; 82 who had received penicillin without reaction and 10 in whom an urticarial type occurred after penicillin treatment. Of 130 patients who received penicillin, 32 had cutaneous lesions; 25 were of urticarial serum sickness type, 7 were of the erythematous-vesicular trichophytid type. Skin eruptions were four times more prevalent in the men than in the women. Pillsbury, Steiger and Gibson (1947) state that urticarial reactions are more frequent in patients who have repeated courses of the drug; they place little reliance, however, on cutaneous tests as a means of predicting the recurrence of reactions with further penicillin therapy. For the treatment of these urticarial reactions they recommend the use of antihistamine drugs by the mouth, such as benadryl, which has proved useful in controlling these allergic manifestations; the treatment by penicillin should be withheld. Willcox (1946) in this country has also tried benadryl with good results.

Herxheimer reactions are reported by Earle Moore (1947) in his monograph as occurring in at least 60 to 70 per cent. of patients treated for early syphilis; with large doses of penicillin, temperatures may rise to 105° F., but in no case has the reaction been alarming. In neurosyphilis and late syphilis the incidence is much lower, there being evidence of therapeutic shock in 20 to 30 per cent. of patients treated.

Callaway (1946) tried graduated doses of penicillin to minimize the risk of febrile reactions; patients received 5 injections of 10,000 units, after which they were given 79 consecutive injections of 50,000 units. In spite of this febrile Herxheimer reactions were frequent, but not sufficiently severe to curtail the course of therapy. Koteen and his colleagues (1947) employing 4 mega-units (25,000 units intramuscularly 2-hourly through the 24 hours) report febrile reactions in 17 patients out of a total of 111 under review. Two tabetics died within two weeks of treatment. Tucker and Robinson (1946) record two cases, in one of whom status epilepticus supervened during penicillin therapy, and the second case, after vomiting several times became extremely restless and excitable. This latter complication of rapid and acute mental exacerbation is of profound significance and Callaway (1946) found in 5 out of 30 paretics treated by penicillin severe mental disturbances requiring sedation and restraint; some became violently agitated and others more grandiose and unco-operative. With a limited experience of 60 cases of general paresis treated by Nicol and Whelen (1947) no febrile Herxheimer reactions were observed, nor was any preparatory course of a heavy metal and potassium iodide given.

OPTIC ATROPHY.

Bruetsch (1946), as a result of the careful microscopical examination of 70 patients with all types of syphilis of the central nervous system, concludes that primary optic atrophy is due to a chronic inflammatory process followed by degeneration of the nerve fibres. The pathological basis, he argues, is more like the process of general paresis than of tabes; it is easier, therefore, to explain the beneficial action of malaria therapy on this disease, malaria thus

arresting the inflammatory process. He advocates a second course of malaria (preferably a different species from that first employed) if failure of vision continues; this might be followed up with penicillin, but the use of penicillin in place of malaria he regards as hazardous. In a subsequent publication (1948) the same author asks the question: Is optic atrophy more frequent in taboparesis than in general paresis? With the histological examination of the visual pathways of 40 patients including both clinical types—27 general paresis and 13 taboparesis—complete optic atrophy was present in 8 cases (4 in each group), but this is not to be regarded as the incidence of optic atrophy in general paralysis, as these cases had been carefully selected with a view to post mortem investigation. (The author, in a previous review of 1,000 cases of general paralysis, found the incidence of complete optic atrophy to be 2 per cent.). On further analysis of the remaining 32 cases, which were not selected, marginal degeneration, ranging from small areas of demyelination in the periphery to large areas of degeneration in the centre of the optic nerves, was found in 62.5 per cent. of the general paralytics, there being no appreciable statistical difference in the two groups. It would appear, therefore, that from this histological review, the pathogenesis of optic atrophy is the same in both general paralysis and taboparesis. The author makes a plea for the more accurate diagnosis of taboparesis; the presence of syphilitic primary optic atrophy as the only neurological sign does not justify the diagnosis of tabes. The explanation as to why only a certain number of general paralytics develop syphilitic optic atrophy is based on the location of inflammation in the sheaths and within the optic nerves; if the latter are not affected, then the visual pathways remain normal. In fact it might be argued that the term taboparesis may well be a misnomer, and that in some cases the diagnosis of general paralysis with syphilitic optic atrophy would be more accurate.

In a review of 54 cases (51 men, 3 women) Levin and others (1947) found that in 34 patients (63 per cent.) the first manifestation of neurosyphilis was gradual loss of vision. Treatment for 43 patients not totally blind was initiated, of these 27 were followed for two years or longer. Fever therapy plus chemotherapy produced far better results in the arrest of the disease process than chemotherapy alone. The authors also found that the arrest of optic atrophy preceded the improvement in the fluid abnormalities. Earle Moore (1947) sounds a warning regarding the use of penicillin only; he reports a patient with early primary optic atrophy, who had been treated elsewhere with 100 intramuscular injections of penicillin (40,000 units) three hourly to a total of 4 mega-units; within three days visual acuity was much worse and at the end of six weeks the patient was completely blind. This disaster is attributed to a Herxheimer reaction, with the advice that it is wise to commence treatment with small doses and gradually increase.

GENERAL PARALYSIS OF THE INSANE (GENERAL PARESIS, DEMENTIA PARALYTICA).

A sign of diagnostic interest in general paralysis is referred to by Reynolds and Moore (1946) in their review of recent literature on syphilis. They quote Thompson, who describes a palmo-mental reflex, which is elicited by stroking

the thenar eminence from the base of the thumb to the wrist; in a positive response the skin on the chin on the ipsilateral side near the midline dimples and moves laterally and upwards. This phenomenon, he claims, is one of the earliest physical signs to appear and though seen sometimes in other neurological disorders, it is far more common in the paretic.

Rashkis (1947) has examined the different types of thinking disorder in three diagnostic categories—schizophrenia, general paralysis and cerebral arteriosclerosis. He employed sorting tests which use verbal and arithmetical materials, and found the differences in these clinical types could be most clearly demonstrated in the relationship between the patient's performance and his explanation of that performance. Schizophrenics perform generally in an operationally "co-ordinated" manner and offer an explanation for their performance; general paretics and arteriosclerotics adopt an "inco-ordinated" manner, and where the former offer no explanation, the arteriosclerotics apologize for their performance. The thinking disorder of the paretic is interpreted as both a deficit in performance potentialities and in organization, whereas though there is a deficit in performance with the arteriosclerotic, the factor of intellectual organization remains unimpaired. Similarly, the Trists (1943) studied the quality of abstract thinking in the treated paretic. They report that specific paretic signs are: (1) Difficulty over initial conceptualization; (2) verbalization difficulty; and (3) form colour sorting. This latter test used in conjunction with ambiguous shapes proved the most diagnostic test in the battery; the authors maintain that on this test alone it is possible to effect a far-reaching separation of general paralytics from the normals and neurotics.

Arieti (1945) provides a critical review of the literature of senile general paralysis together with a clinical and pathological description of six cases. Patients in whom symptoms appear for the first time at the age of 60 or over are classified as senile general paralytics. For the decade 1932-1941 the incidence of this senile type among G.P.I. admissions to the New York State Hospital was 10.58 per cent.; the disproportion between male and female was even more pronounced in senility. The symptomatology was that of an organic psychosis; hallucinations were absent, all cases showed behaviour disorder and in only one case were grandiose delusions present. The irregularity of the findings of the cerebrospinal fluid made diagnosis difficult; the course of the disease was rapid with progressive deterioration. The crippling nature of general paralysis with the consequent loss to the community is referred to by Iskrant (1945). He estimates that as a result of hospitalization of general paralytics in institutions in New York State the annual loss of working years of life is 75,729 man years and 23,645 woman years; this involves an estimated money loss of income for men of approximately 112 million dollars. Even with many patients, in whom treatment arrests the disease process at a high level, the earning capacity is seriously impaired. But Whelen and Bree (1946) in this country make a plea for a wider conception of the promotion of optimum health—"the criterion of successful treatment is the degree of satisfactory functioning of the patient in society."

M. Lomholt (1944) has written a most interesting catamnestic study

of 579 cases of general paralysis treated by malaria at the Hans Hospital, Copenhagen. The investigation was carried out with extreme efficiency, 99.5 per cent. of the patients were traced after intervals of from 4 to 17 years; the report deals with males only. The report is too long to summarize in detail, but a close study of the tables presented furnishes much valuable information. The question as to how far modern syphilotherapy (salvarsan) might have influenced the subsequent development of symptomatic neurosyphilis is discussed. While the average incubation period of general paralysis has increased from 15 to 21 years, the author is loth to attribute this to the effect of improved treatment for early syphilis; she quotes Abely, who points out that the mean incubation period calculated over a certain period depends on the increase or decrease of the syphilis morbidity during that same period. In a period of increased syphilis morbidity, the incidence of general paralysis will increase too, but during the first years only will cases with a short incubation period become manifest. So over a ten-year period of high syphilis morbidity there will be many cases of general paralysis with a short incubation period, thus decreasing the mean for this time. With a decreasing syphilis morbidity the incidence of general paralysis will decrease too, but over a ten-year period there will be a reduction of short incubation cases, but added to this incidence will be the long incubation cases from preceding years with a high syphilis morbidity, the mean, therefore, being artificially increased for the time under review.

In the material reviewed only 78 patients are known to have had salvarsan for the primary and secondary attack; moreover, in the records available, there is no evidence of a single patient receiving antispecific treatment adequate by modern standards. The clinical types observed on admission to hospital are classified into three main groups: 82 were of the neurasthenic, slightly demented type; 100 were of the grandiose, expansive variety, while 414 were fatuous and euphoric with dementia; no mention is made of those cases where confusion is a predominant symptom, nor of those admittedly rare, who are profoundly depressed.

The clinical results are very well tabulated and the description "improved" is purposely avoided, as the term is far too relative. The clinical results are divided into 7 subheadings: Group 1, recovered without defect; (2) recovered with slight defect, able to work; (3) stationary, demented, partly able to work; (4) stationary, demented, unable to work, "family nursing home patient"; (5) stationary demented hospital patients; (6) third stage of progressive paralysis; (7) deaths. Sixty (10 per cent.) of the 576 patients recovered without defect; 68 (12 per cent.) recovered with a slight defect. It was found that if a patient remained in Group 1 for three years it could be anticipated that he will remain in that group for the rest of his life.

The author deplores the delay in arriving at a diagnosis, with the result that too many patients are submitted to treatment when irreparable damage to the cortex has been wrought.

Another feature of considerable clinical interest described by Lomholt is that of the hallucinatory psychosis with its schizophrenic-like behaviour; she produces evidence which does not support the view held by some workers that it is an extremely rare phenomenon and a product of malaria therapy. In her

series 113 were hallucinated prior to treatment, 36 became hallucinated for the first time during treatment, and 48 developed hallucinations after treatment. Among 107 who did not receive treatment, 39 were hallucinated. The additional factor of alcohol was stressed, in 176 out of 686 cases chronic alcoholism was noted. Gerstmann has long drawn attention to a paranoid hallucinatory picture as coming on as a sequel to malaria therapy. It is more likely, however, that in some cases general paralysis is superimposed on an already existing schizophrenic process and that it is the beneficial effect of malaria which arrests the neurosyphilitic process, thereby unmasking the presence of the paranoid hallucinatory psychosis. Woolley (1945) draws attention to the fact that this syndrome occurring in relation to general paralysis tends to persist and to be irreversible; this is in contrast to the view that the toxic effect of malaria precipitated the condition. Dattner (1944), in his book, reviews the literature on the subject, but he puts forward the theory that some toxic factor is responsible. He suggests two factors: (1) A constitutional predisposition and (2) depressed liver function caused by chronic or acute intoxication, the former being the result of chronic alcoholism or prolonged arsenotherapy and the latter due to some vigorous therapy, such as malaria. There seems to be general agreement that the occurrence of this syndrome is of serious significance and it may well persist.

ELECTROENCEPHALOGRAM IN NEUROSYPHILIS.

The presence of EEG abnormalities in neurosyphilis is described by Greenblatt and Levin (1945). Out of 300 cases of neurosyphilis, 233 were selected for investigation; in 50 per cent. the EEG was abnormal (46 per cent. abnormal slow; 44 per cent. abnormal fast, and 10 per cent. paroxysmal). A control group of 240 doctors, nurses and auxiliary staff were also tested and 10 per cent. of this group showed abnormal waves. The incidence of abnormality in the neurosyphilis group according to clinical types was highest in meningovascular syphilis (60 per cent.), in general paralysis it was 55 per cent.; optic atrophy 44 per cent. and tabes 14 per cent.; the tabetics were not significantly different from the control group. In the clinical group 20 per cent. of total cases gave histories of cerebral seizures, as compared with 1 per cent. in the normal population. In the general parietic group the highest incidence of abnormal EEG occurred in those cases with seizures, the next highest in those with marked tremors and dysarthria, so there is some correlation between the EEG abnormality and the clinical condition. No correlation was found with regard to the presence of pupillary changes, delusions or hallucinations. The high incidence of abnormality found in optic atrophy is unexplained. These authors report that with clinical improvement as reflected by a healing of the cerebral condition, the pattern of the EEG showed a similar approach to normal. Callaway and his co-workers (1945) studied the EEG of 38 patients suffering from neurosyphilis, including 26 general paralytics and 7 taboparalytics. After penicillin treatment (4 mega units in 10 days) they found that many formerly abnormal EEG became normal, while others improved. They advance the theory that the abnormality is "an expression of local anoxia and a generalized or localized cerebral inflammation." Similarly, Scott and Gammon (1946)

found the improvement in abnormalities in the EEG a useful method in evaluating the effect of penicillin; they report their findings in 30 cases, of whom 10 were paretics and 9 taboparetics.

MALARIA THERAPY.

For the medical historian a debt of gratitude is due to Bruetsch (1946), who published a manuscript written by Wagner-Jauregg in 1935, on "The History of the Malaria Treatment of General Paralysis." Wagner-Jauregg describes how he conceived the idea of giving mental patients malaria or erysipelas as far back as 1887. The idea of giving malaria was not pursued; erysipelas was tried with poor effect, but in any case was not applied to cases of general paralysis. He then turned his attention to tuberculin, and in 1909 reported with great caution some moderate success with general paralysis; moreover, he maintained that an elevated temperature was not the fundamental factor in treatment. Tuberculin treated cases were liable to relapse, and again Wagner-Jauregg was attracted by the idea of employing malaria. It was in June, 1917, that "a sign of destiny" presented itself. A wounded soldier returned from the Balkan front, had an attack of malaria and this was reported by Wagner-Jauregg's assistant, quinine was withheld, the diagnosis confirmed, and the blood of this soldier was used for scarifying the arms of three general paralytics; two developed fever, and so the first cases on record received malaria therapy.

Kitchen and Putnam (1946) give a useful analysis of the character of the paroxysm observed in *P. vivax* malaria. They report an average of five days' clinical activity before the first rigor occurs; the incidence of rigors is 51 per cent. for attacks up to three weeks' duration. An interesting point noted by them is that in 654 paroxysms accompanied by rigors, the mean maximum temperature was 104.2° F., compared with 102.5° F. in 346 rigorless paroxysms.

Read, Kaplan and Becker (1946) published a useful account of clinical complications observed during malaria therapy. An analysis of 300 cases is reported; 211 were treated with *P. vivax*, and 89 with *P. malariae*. The chief complications referred to are jaundice, oedema and mild renal damage. Jaundice was reported in 22 cases, the incidence being slightly higher in those patients treated with quartan malaria. Of 4 cases of acute nephritis, 3 were cases of quartan. 50 per cent. of the jaundice cases in the absence of impaired liver function are accounted for by excessive haemolysis, which is almost certainly the result of a high parasitaemia. This is a pointer for the need to carry out regular parasite counts on patients during malaria therapy. At the Horton Malaria Therapy Centre, where a series of over 2,000 cases has been treated, the incidence of jaundice has been extremely rare. This is probably attributable to the fact that when parasite counts, which are done daily, reveal a high parasitaemia, fever is temporarily interrupted. An unusual form of severe respiratory distress with cyanosis was observed in two cases with a quotidian fever, both treated by benign tertian malaria; no further difficulty was found following administration of thiobismol.

Liver function tests during malaria therapy have been carefully studied at two clinics, Glenn, Kaplan and others (1946) and Lippincott and others (1946).

Glenn and his co-workers found the liver to be palpable in 24.7 per cent. of cases at some time during the clinical course. It appears that the liver is involved in every case of malaria, showing some dysfunction by various tests; the involvement is probably not severe, as most tests return to normal soon after termination of malaria. These workers tried the effect of diet in protecting the liver against possible damage; additional protein had little effect, but intravenous glucose therapy lowered the incidence of liver enlargement quite significantly. A point of interest brought out in their work was the fact that the number of hours of fever above 103.6° F. was very much higher in the quartan group, compared with benign tertian malaria.

From the Liverpool School of Tropical Medicine in this country some interesting work has been carried out on the pathological processes and liver lesions in malaria by Maegraith (1948) and Horner Andrews (1948). Andrews, in his studies of liver lesions from necropsies (in human malignant tertian malaria and monkey malaria), concludes that the lesions of the liver, like those of the brain, are an example of the effects of tissue anoxia. Maegraith's approach is largely from a physiological angle; his work is confined to studies on *P. falciparum* malaria, and he refers to the profound circulatory changes sometimes met with, which are indetical with those of severe shock. "The skin is cold and moist," he says, "the pulse is rapid, thin and easily compressed, and the respiration superficial and irregular. The blood pressure is low and there is haemoconcentration and other evidence of acute reduction in blood volume." He maintains that there is local loss of fluid in many tissues due to damaged vascular endothelium, possibly the result of a tissue anoxia. Nicol (1948), in a discussion on Maegraith's paper drew attention to similar catastrophes with signs of peripheral failure occurring in cases of *P. vivax* malaria. Though such cases are fortunately rare, they are extremely alarming and give rise to considerable anxiety. The treatment for this condition, Maegraith states, is that for all forms of medical shock, whether caused by malaria or other disease; the primary object is to restore the circulatory blood volume, and parenteral administration of glucose saline or plasma is indicated.

Rigdon and Varnadoe (1947) report experimental work on ducks infected with *P. lophurae*. They found that ducks died from lesions similar to those of shock. By putting the highly parasitized ducks in an oxygen chamber when they had developed anaemia, weakness and a rapid respiratory rate, immediate improvement was observed. On this analogy they discuss the use of oxygen in the treatment of acute malarial infections in man.

Other rare complications in malaria therapy are purpura and spontaneous rupture of the spleen. Reynolds and Moore (1947) refer to a paper by Moses, who recorded a case of splenic rupture where early recognition of the condition and prompt surgical intervention saved the patient's life. Greco and Ziedman (1944) report a severe case of purpura occurring during a course of fever, induced by quartan malaria; fever was terminated, but in view of the patient's severe clinical state, blood transfusion had to be given. Shrager and Kean (1946) discovered 9 cases of purpura complicating malaria in a series of 10,000 treated for malaria; every case occurred after treatment with quinine, which was at once substituted by atebrine. The presence of active pulmonary

tuberculosis or even a history of such disease has been regarded by nearly all authorities as a contraindication for malaria therapy. In spite of this, Pleasure (1944) treated with malaria 11 cases of general paralysis with tuberculosis; in only one patient did the pulmonary lesion spread, two died of advanced G.P.I. but not from the tubercle. The author admits the risk, and suggests it is not the fever which is dangerous, but the exhaustion caused by excessively rigorous treatment. For this reason he prefers quartan malaria to benign tertian.

Malaria therapy may undoubtedly be a dangerous procedure, but the use of thiobismol, first described by Schwartz (1939) in America and Whelen and Shute (1943) in this country, is of great value in minimizing the risk. The relative certainty with which it is possible to convert quotidian into true tertian fever in *P. vivax* infections by the use of this drug, coupled with the possibility, should an emergency arise, of being able to stop the attack within 24 hours by the simultaneous administration of thiobismol and a recognized anti-malarial, such as mepacrine or quinine, has made the treatment comparatively safe.

A question that is often asked is whether the incidence of neurosyphilis is lower among inhabitants of endemic malarious areas. Martin J. Cook (1948) examined the cerebrospinal fluids in an unselected group of 1,028 patients from Trinidad, excluding cases of yaws with care. Positive fluids were discovered in 153 cases (14.9 per cent.); 126 with minimal changes, and 27 showing marked abnormalities. Clinical records of 527 of the total patients were examined and the cerebrospinal fluid results are correlated with the final diagnosis; 82, or 15.5 per cent. were diagnosed as suffering from neurosyphilis, 48 with the asymptomatic type and 34 with the symptomatic disease, in which latter group were 13 tabetics, 5 paretics and 8 cases of optic atrophy. By eliminating 110 of these with a history of yaws, 417 remain who were considered syphilitic. On this basis the incidence of asymptomatic neurosyphilis (48) is 11.5 per cent. and that of the symptomatic type (34) is 8.5 per cent. The clinical records of 501 patients were not correlated with the fluid findings, and in this group 73 (14.6 per cent.) had positive fluids; the authors postulate that this result is so close to the more carefully analysed group that it is probable the clinical types would have been similar. Though the severity of the type of neurosyphilis may be somewhat tempered by the presence of endemic malaria (malaria rates of 20 to 80 per cent. existed in some areas from which the patients were drawn) the authors conclude that the neurosyphilitic rate among negroes compares fairly well with that among whites in colder climates.

TRYPARSAMIDE.

While the view is largely accepted that for the treatment of late neurosyphilis pentavalent arsenicals are superior to trivalent preparations, Koteen (1947) quotes experimental work and concludes that there is little satisfactory evidence that tryparsamide possesses either greater penetrability or affinity for the central nervous system than the trivalent arsenicals. In the evaluation of any drug the author asks two primary questions: (1) Its toxicity and (2) its therapeutic efficiency. He proceeds to quote the evidence of numerous workers, which

leave the impression that tryparsamide is not only toxic and dangerous, but a feeling of surprise that physicians have used it so extensively. Koteen then proceeds to give a detailed review of 736 patients with asymptomatic neurosyphilis and 355 tabetics treated at the New York Hospital. In the asymptomatic group, 206 were followed up for a period of from one to six years; 139 of them received tryparsamide during the course of antisyphilitic treatment, 60 (43 per cent.) developed toxic reactions of such a degree that the drug had to be withheld. 45 of the 139 (32 per cent.) developed subjective evidence of optic nerve sensibility and subsequent observation showed that 17 were left with permanent visual damage. In the 355 tabetics, 202 were followed up for a period of 5 to 8 years; 126 received tryparsamide and 22 showed minor toxic reactions, nitritoid, gastrointestinal upset and dermatitis. The development of symptoms affecting the optic nerve was far more serious; of 59 patients so affected, 27 had objective evidence of optic atrophy, resulting in impaired vision, 27 recovered entirely, but 5 became blind. With regard to its value in general paralysis the author is inconclusive, as most cases received malaria, or more recently, penicillin, as well.

Potter (1943) refers to the acute type of reaction as opposed to the chronic type of visual deterioration. He states that the acute reaction, with far more serious consequences, only occurs in less than 1 per cent. of patients receiving tryparsamide therapy and that it usually appears after the first few injections and bears no relation to the amount of drug injected. Nicol (1946), who reports results of malaria plus tryparsamide from the Horton Malaria Therapy Centre, in a series of 217 cases found that 10 patients exhibited toxic symptoms. This incidence is low, but the course of tryparsamide administered was small, 22 gm. Nevertheless, one had nitritoid reactions, one jaundice, 8 misty vision, 2 of whom were blind for several days, but fortunately recovered their sight, though it was seriously impaired; in all cases reported, toxicity was detected before three injections had been given. The risk of permanent damage to vision is undisputed; how far the discovery of BAL can reduce or counteract this danger is uncertain. Friedenberg (1947), however, reports the successful use of BAL in a patient with tabes, who, after two small doses of tryparsamide (0.7 gm. and 1 gm.), complained of blurring or a shimmering of vision.

Another pentavalent arsenical preparation, alvarsone, has been tried in the treatment of neurosyphilis. Goldman (1947) used this drug at weekly intervals of 1 gm. doses for 20 weeks in conjunction with induced artificial fever in a group of 58 general paresis. He reported no nitritoid crises, no skin eruption and a total absence of any damage to the optic tract. The reduction of the cell count and protein in cerebrospinal fluid was rapid, though it must be pointed out that adjuncts in fever therapy and bismuth were employed.

Eisenberg and Hershfield (1948) report their findings in 100 patients with various types of neurosyphilis who received 1 gm. alvarsone and 1 c.c. bismuth salicylate concurrently over a period of 24 weeks once a week. 41 cases were asymptomatic and 59 symptomatic neurosyphilis. A negative fluid was obtained in 12 patients and 58 showed a reduction; no toxic reactions were reported. The authors conclude that the treatment is a safe ambulatory procedure.

CHEMOTHERAPY AS AN ADJUNCT TO MALARIA THERAPY OR ARTIFICIAL FEVER.

Whether the case to be treated is suffering from asymptomatic neurosyphilis, meningovascular neurosyphilis, or the more severe parenchymatous infection, the aim of any form of therapy is to arrest the progress of the disease and to convert an active fluid to one of inactivity or better still to produce a complete reversal. It has already been pointed out that the type of fluid abnormality is a useful index in deciding the method of therapy required.

In those cases with group I or group II fluid abnormalities a course of chemotherapy, or treatment by fever, is generally adequate in achieving a cure. But with patients with a group III fluid, whether asymptomatic, or suffering from clinical symptoms, such as general paralysis, tabes or taboparesis, it would appear that most authorities are agreed that a combination of methods produces better results than a single therapeutic procedure.

Dattner (1944) and his colleagues reviewed a series of 419 cases who were treated between January, 1939, and June, 1943. The clinical material comprised 125 asymptomatic cases, 35 meningovascular neurosyphilitics, 74 general paralytics, 103 tabetics, 34 taboparetics, 32 tabetics with optic atrophy, and 16 congenital neurosyphilitics. Of this group 148 were treated with malaria plus routine chemotherapy, 276 with malaria plus 0.06 gm. mapharsen daily for 10 days; (5 were re-treated with malaria). Routine chemotherapy included weekly injections of arsenical drugs followed by bismuth for six months; the mapharsen treatment was limited to 10 days and was given immediately after the last day of fever. In the follow up 62 were untraced, 10 died and 54 were too recent for evaluation. The report was limited, therefore, to 293 patients, who had been under observation from 6 to 48 months after treatment was terminated. Comparing the results of these two modes of treatment it was found that patients whose chemotherapy following malaria was limited to 10 days did quite as well as, or better than, those who received at least six months' routine injections of arsenic and bismuth. The advantage of completing the therapy while the patient was still in hospital and so avoiding the inevitable delinquencies which occur during routine weekly injections cannot be overstressed.

Nicol (1946) reviewed two series of 217 cases, 127 men and 90 women. With the exception of 25 congenital cases of general paralysis, all the other cases were acquired general paralysis or taboparesis. The first series was treated by malaria alone, the second group received a supplementary course of tryparsamide, 22 gm. in eight weekly injections immediately following the malaria. The period of follow up varied from ten to twelve years, and even with the discharged patients a high proportion had been contacted. Though malaria alone will arrest the disease process and in some cases effect a cure both clinically and serologically, there was a striking difference between the two series. Decidedly better clinical and serological results were obtained in cases treated with both malaria and tryparsamide than in those treated with malaria alone; over the period under review 9 per cent. more cases were discharged and 20 per cent. fewer died.

In an article on the present status of treatment of general paralysis Marsh (1944) reviews the work of various authors. While artificial fever is preferred

to malaria by some, there seems to be general consensus of opinion that the addition of chemotherapy offers the highest incidence of remission among patients when used following fever therapy.

The use of penicillin has certainly revolutionized the treatment of neurosyphilis, but as already mentioned there is considerable conflict of opinion as to its superiority to the older methods of treatment. Dattner (1948), who has had a wide experience of malaria, in his latest publication definitely champions the cause of penicillin. "I am convinced," he writes, "that at present penicillin in adequate dosage is the most convenient and effective treatment for all types of neurosyphilis." This is a bold conclusion, and time alone will confirm the correctness of such a statement.

Malaria therapy has been in use in this country for over a quarter of a century; has the time come for it to be superseded? In the case of early optic atrophy are we justified in telling the patient that he need not have malaria, penicillin will arrest the progress of the disease equally well?

That penicillin is a useful adjunct to malaria, no one will deny; Nicol (1946) suggested that it might well replace the use of tryparsamide in conjunction with malaria. Rose (1948) and his co-workers recommended that where penicillin and fever, were employed, the amount of fever, whether malaria or fever cabinet, could be reduced approximately by one half of the total amount which by old criteria would have been necessary. Lescher and Richards (1947), with admittedly small numbers, tried to evaluate the results of three methods of treatment—malaria plus penicillin, penicillin alone, and malaria with chemotherapy. They found the best clinical and serological results were obtained by malaria with penicillin. Similarly, Reynolds, Mohr and Moore (1946) report the superiority of penicillin plus malaria over penicillin alone. Chesney and Reynolds (1948) treated a series of 54 tabetics, 33 with penicillin alone and 21 concurrently with penicillin and malaria. They found a clear-cut superiority for combined therapy. Curtis and Burns (1947) followed up 118 patients with various types of neurosyphilis, including a fairly high proportion of taboparesis and general paralysis; 75 were treated with penicillin and 43 with penicillin plus malaria. The minimum period of follow up was one year. These authors found a clinical superiority of 23 per cent. and a laboratory superiority of 19 per cent. where the combined method rather than penicillin alone was utilized. Bennett and Hargrove (1947), who advocate artificial fever, combined this with penicillin; though the numbers were too small for comparison with their earlier series treated with physical fever, bismuth and mapharsen, they found the penicillin fever treatment results were not so good; in active clinical neurosyphilis, general paralysis and tabes, they maintain that penicillin should not be relied on alone.

It will be some years before we are in a position to be dogmatic about penicillin. The dosage recommended varies within wide limits; we do not know whether the preparation in beeswax is a more effective therapeutic agent. Experimental work suggests the concurrent use of penicillin and malaria as being more efficacious than malaria followed or preceded by a course of penicillin. These are all problems which need careful investigation and elucidation.

Whatever régime is adopted, early diagnosis and the immediate inception of the appropriate treatment can afford the only means of checking the disease. O'Leary (1937) wrote: "I still believe that malaria is of more value in the prevention of general paralysis than it is in the treatment of it." This remark may well apply to penicillin too, and if it is realized that clinical neurosyphilis is a preventable disease, the hazards and crippling disabilities of general paralysis, tabes and optic atrophy would disappear.

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EPILEPSY.

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IN his presidential address to the twenty-sixth annual meeting of the Association for Research in Nervous and Mental Disease, Lennox (1947a) estimated the epileptic population of the world at about 10,000,000, for 6,000,000 of whom only the most primitive therapy is available, and no more than 300,000 are receiving investigation and treatment by modern methods. The various fields in which advance is being made may appear widely separated but the boundaries between them are ill-defined, and the aim must be towards integration. Thus, there is the approach to investigation and classification through the varied clinical types of fits, through cerebral anatomy and cerebral localization, through the fundamental aetiological division into symptomatic and essential (Lennox prefers the terms "acquired" and "genetic"), through E.E.G. patterns, through the physical and chemical changes that underlie neuronc metabolism and their modification by drugs, and through the study of associated mental changes and social reactions. In most of these fields, progress is now more rapid than at any former time.

BOOKS.

Penfield and Erickson's important work on *Epilepsy and Cerebral Localization* (1941) provides a comprehensive account of fits arising from focal lesions, their surgical treatment and deductions about the localization and nature of cerebral function that may be derived from their study. The account of idiopathic epilepsy is less satisfactory. Two collections of papers on epilepsy have recently appeared. One gives *in extenso* the *Proceedings of the Association for Research in Nervous and Mental Disease*, held jointly with the International League against Epilepsy (1947), and presents a stimulating and encouraging picture of advance on many fronts. The other, of less importance, is edited by Hoch and Knight (1948), and is a collection of papers presented at the annual meeting of the American Psychopathological Association. Two little books by Lennox (1946a) and by Tracy Putnam (1945) give an account of epilepsy designed for reading by the general public. A review of the world literature is included each year in *Epilepsia*, the annual publication of the International League against Epilepsy. Temkin's monumental work on *The Falling Sickness* (1945) gives a well-produced and well-documented account of the history of epilepsy, from the Greeks up to and including the time of Hughlings Jackson. It will remain a standard work long after all the books and articles referred to in this review have been superseded.

INCIDENCE.

Endeavours to estimate the incidence of epilepsy have yielded notoriously inconsistent results. Difficulties of definition are almost as great as difficulties of ascertainment. Malzberg (1948) gives some account of the American Army

figures, the validity of which seems to have been generally accepted. In the first World War, among over 2,000,000 men between the ages 19 and 31, 5.15 per 1,000 were rejected on account of epilepsy, the rejection presumably being largely based on clinical history. As Malzberg points out, the number should probably have been larger, as, when the history was omitted or denied, the epileptic would have got through the net. (One may be allowed to suggest that it should also be smaller, by reason of invented histories.) The value of the figure is a little discounted by its extraordinary variability in different districts, from 1.2 to 12.7 per 1,000, the rural-urban ratio being 112 to 100. To the 5.15 per 1,000 rejected for entrance to the services must be added a further 1.85 discharged from the services on account of epilepsy. Even the high figure of 7.0 per 1,000 is not complete, as it presumably takes no account of institutional epileptics. Similar, but as yet incomplete, figures are being found in the second World War. In the application of these findings to the general population we are on less sure ground. Sex may be disregarded as a disturbing factor, as there is general agreement that the number of male and female epileptics is approximately equal. But in the age groups below 19 the incidence of epilepsy is likely to be higher, and above 31 lower than in the special group reported on.

Confirmatory evidence along similar lines comes from Canada, where Sheps (1947) finds an incidence of 3.9 per 1,000 among recruits between the ages of 18 and 40, but this number also includes those whose fits were first observed when they were serving soldiers. Sheps adds the number of epileptics of military age in institutions in the part of Canada under review to make a total of 5.5 per 1,000 for the adult male population.

One in 200 appears to be now generally accepted as the epilepsy rate, compared with 1 in 500 a generation ago, but we cannot reasonably take the former figure as final. There is no agreement as to how many fits must occur before a diagnosis of epilepsy is justified, how many years of freedom must elapse before an epileptic ceases to be an epileptic, which of the borderline conditions should be scheduled as epilepsy, and other very relevant problems.

ELECTROENCEPHALOGRAPHY.

The E.E.G. now occupies a unique place in the study of epilepsy. There is no field of research in which it is not implicated, and as E.E.G. work develops, new avenues for investigation are continually opening up. A general account of the relationship between epilepsy and the E.E.G. has recently been given by Jasper (1948). He states that the E.E.G. has not only established its value in diagnosis and treatment, but is a most useful tool in the investigation of the nature of epileptiform disturbances. It has provided a new method for classification, a sensitive indicator of inter-seizure subclinical discharges, and a method of detecting related disturbances in non-epileptic individuals with latent epilepsy. It has made possible the objective demonstration of genetic predisposition in the relatives of epileptic patients. It permits the observation of the focus of onset and march of the epileptoid process from one area of the brain to another. Finally, it has broadened the field to include many disorders of thought and behaviour in patients who have

never experienced a true convulsion. These include not only recognized "equivalents," but also certain psychopathological states covering a wider field. At the same time, it is well to remember that the E.E.G. is not more than a means of electrophysiological observation, and must only be correlated with clinical manifestations and biochemical changes with great caution. Epileptiform activation is represented by sudden bursts of high-voltage waves, and thus is the opposite of normal activation in which there occurs a decrease in voltage of resting rhythms due to dys-synchronization. Jasper cites six fundamental characteristics of the epileptic discharge: (1) High-voltage discharges, or hypersynchrony. (2) Autonomous activity, usually self-initiated and always self-perpetuating. (3) Spread of focal discharge, both along neuronal pathways and by direct activation of adjacent tissues. (4) Relation with the afferent system. Afferent stimuli may cause arrest, as when the eyes are opened in the course of a wave and spike discharge from the occipital regions, or facilitation, e.g. in reflex epilepsy, or fits occurring in response to emotional stimuli. (5) Relation with the efferent system. This is obvious in the major fit, but subclinical discharges also send impulses along efferent channels. (6) Relation to the integrative action of the brain, resulting from the loss to the patient of adaptive and integrative functions of any area of the brain occupied by epileptic discharge. The E.E.G. has emphasized the distinction between symptomatic and idiopathic epilepsy. The establishment of a single cortical area of onset at once suggests the former, and here random rhythmic discharges will be seen in inter-seizure periods. Of these, random spikes are the most important, and may be regarded as the *sine qua non* of a superficial cortical focus, often being localized in a very small area and typically lasting for from 5 to 10 m./sec. Somewhat similar surface negative waves, lasting up to 200 m./sec., are called sharp waves, and are of less diagnostic significance, while the commoner slow, or delta waves, are indicative of damaged cortical tissue, not necessarily epileptogenic. Lesions on the mesial and inferior surfaces of the brain have less clear-cut E.E.G. accompaniments, while deep-seated lesions often cause bilateral rhythmic disturbances indistinguishable from those seen in cryptogenic cases. In the latter, two principal groups of discharges are observed: (1) Bilateral synchronous discharges arising from homologous areas of the two hemispheres. (2) Diffuse relatively disorganized discharges arising from many cortical areas on both sides. The principal features in these groups are the wave and spike complex, high-voltage fast rhythms, and the diffuse, slow and sharp wave patterns. Bilaterally synchronous slow and sharp waves are not so specific for epilepsy as the wave and spike complex, but are often the only type of disturbance seen in the near relatives of patients with idiopathic epilepsy, and may therefore represent a latent type of the disorder. It must not be forgotten that E.E.G. patterns can be closely simulated by toxic or metabolic factors, by post-encephalitic conditions and by deep-seated local lesions. Since the E.E.G. forms of discharge are the same from superficial lesions of any area, it is clear that the type of seizure in focal epilepsy is determined by localization and paths of spread. Jasper accepts the findings of Gibbs and Lennox, that different electrical patterns are associated with the three main types of seizure,

i.e. continuous high-voltage fast waves followed by interrupted bursts in major fits, alternating fast and slow (spike and wave) in *petit mal*, and 6 per second flat-topped waves in many cases of psychomotor epilepsy. These are all bilaterally synchronous, and seem to involve principally the motor areas, the frontal areas and the temporal or fronto-temporal areas respectively.

The relation, however, between clinical attack and E.E.G. picture is not clear cut. A major fit may often be preceded by wave and spike complexes, less commonly high-voltage fast waves precede a typical *petit mal* attack, while 6 per second flat-topped waves can frequently be seen in patients who have never had a psychomotor fit. Jasper is inclined, therefore, to think that the differences between the varieties of attacks are quantitative rather than qualitative. Finally, he refers to the suggestion made by some E.E.G. records that certain confusional states, impulsive and irrational behaviour, and some psychotic or psychoneurotic reactions may be of an epileptoid nature. Sometimes marked improvement follows the use of anti-convulsant therapy suggested by the E.E.G. findings.

An independent study of the E.E.G. in relation to epilepsy has been made by Frey (1946). He presents full clinical histories and laboratory and E.E.G. reports on 159 cases of epilepsy, 53 of suspected epilepsy, 120 of non-epileptic abnormality and 101 controls. He finds that a slow alpha frequency in bi-occipital leads is suggestive of a brain lesion (whether the subject has epilepsy or not), and also of an epileptic type of personality. Also suggestive of both epilepsy and the epileptic personality are a large amount of continuous slow activity, under 6 per second in antero-posterior and transverse leads, of 6-8 per second activity in precentral-occipital leads and, of course, of bursts of activity. Most highly suggestive of all is the wave and spike complex. Fast activity of 15 per second or more, he finds of little diagnostic value. Focal abnormality means a brain lesion, and, if fits are present, indicates their origin. In this detection of focal origin lies the primary value of the E.E.G. in epilepsy. As an aid to the differentiation of epilepsy from other attacks of undecided clinical nature, it does not possess diagnostic value, but is a useful adjuvant.

The finding of abnormal records in neurotic and psychotic patients who have never had fits, the variability of the pattern in response to chemical change and the inverse ratio that exists between age and abnormal E.E.G., have led some to cast doubts on the validity of the E.E.G. in diagnosis. It is probably true to say, however, that there is now general agreement that spike and wave complexes, and their slow and fast variants, are pathognomonic of epilepsy, and that paroxysmal outbursts of fast (12 or more per second) or slow (less than 4 per second) waves and of spikes are very suggestive of epilepsy, and, taken with the clinical history, will often lead to a positive diagnosis.

Several workers have commented on normal E.E.G.'s in known epileptics. Among 195 epileptics Abbott (1947) found 21 per cent. with normal, and a further 10 per cent. with doubtfully abnormal, records. Analysis shows that among the 69 per cent. with definitely abnormal records the age of onset is earlier, fits are more frequent, the response to medicine is less satisfactory and social difficulties more prevalent. Those who have major fits only, or whose

attacks are confined to the night, are more likely to have normal records. Family history, the occurrence of convulsions in infancy, or the presence of a focal lesion, do not appear to affect the incidence of normal E.E.G. records in epileptics.

The number of epileptics with normal E.E.G.'s would be greatly reduced by systematic recording during sleep. This procedure has been carried out by Gibbs and Gibbs (1947), who took E.E.G.'s of 500 epileptics and 90 controls, both sleeping and waking. They find seizure discharges rare during sleep in normal people, but twice as likely to appear in epileptics when asleep as when awake. If, during a subclinical *grand mal* attack in sleep, the patient is roused, a clinical major fit supervenes. The incidence of seizure discharges is higher in symptomatic than in idiopathic epilepsy, both in sleeping and waking hours. Discharges of the psychomotor type are particularly liable to be absent awake, and present asleep; they are usually focal in the temporal area. Other foci that are invisible awake often declare themselves during sleep. Sleep studies more than double the value of the E.E.G. (they are especially valuable during light sleep), and are less disturbing for the patient, less laborious for the physician and more effective in precipitating abnormality than the induction of hypoglycaemia, hydration or activation by metrazol. Fuchs *et al.* (1948) produced sleep by administering pentothal to 40 patients with psychomotor epilepsy. Pentothal stimulates subclinical seizure discharges, and in every case the characteristic anterior temporal focus of spikes was produced. The procedure is simple, and is likely to be useful when operation is called for, as pentothal serves the double purpose of an anaesthetic and a focus activator.

Another method of evoking E.E.G. abnormalities in patients with normal records is by the intravenous injection of insulin. Baisset *et al.* claim that this is effective even among older patients, and that with a rapid fall in sugar and a short period of hypoglycaemia, abnormalities are not seen in normal people.

A comparison of the E.E.G. records of 300 institutional with those of 750 non-institutional epileptics has been made by Belinson (1947). The average age of the institutional cases was 33, and the average I.Q. 69. Some degree of mental defect, therefore, was often associated with the epilepsy.

There was a history of major fits in almost every case. Admission to institution had been called for by poor socio-economic conditions, broken homes, conduct difficulties and the like. The E.E.G. records, considered *en masse*, show marked differences from those of the ordinary run of extramural epileptics. There are paroxysmal records in 47 per cent of the group, as compared with only 29 per cent. of the general epileptic population, the increase being marked in the *petit mal* variant, and still more in the psychomotor type of response. By E.E.G. standards, indeed, psychomotor manifestations are three times as common in institutional epileptics, and Belinson takes this to mean that psychomotor epilepsy is the basis of the difficult behaviour problems which lead many of these patients to find their way to an institution. In inter-seizure periods very slow frequencies are markedly increased in the institutional group, whose E.E.G.'s also show a greater degree of irregularity, more fluctuation of voltage and an unusual mixture of frequencies.

PITRESSIN TEST.

The greater proportion of negative E.E.G.'s in cases of clinical epilepsy as age advances has led to the use of pitressin in service cases of doubtful diagnosis. As Dick (1947) points out, a rapid decision under service conditions is essential to avoid (1) wasting time in further training for a man who will be discharged if he has epilepsy, (2) sending a man out into the world with an epileptic label attached without definite proof of epilepsy, and (3) making mistakes about attacks arising out of a desire to evade service. He presents the results obtained in the attempt to come to a diagnosis in 164 service cases with unsubstantiated histories and without physical signs. The group was analysed in three ways. First, such clinical evidence as was available was assembled, and the cases classified as definitely epilepsy, probably epilepsy, and improbably epilepsy. Then an E.E.G. was performed on each man, the results being classified according to the criteria laid down by the British E.E.G. Society, into pathognomonic (there were none in this group), very suggestive, non-specific, and negative. Finally, the pitressin test was administered. Half a pint of water was given to the patient every two hours, and injections of pitressin (5 units), followed by 10 units every four hours for 40 hours. The E.E.G. and pitressin results were correlated with the provisional clinical diagnosis. At least 6 months later, after the man had left hospital, the position was re-examined. By that time the clinical diagnosis had, in many cases, become clear, and the value of the original provisional classification, and of the E.E.G. and pitressin test findings, could be seen. The figures show that, of the three, the clinical diagnosis easily takes first place, and the pitressin test is a good deal more helpful than the E.E.G.

A combination of the pitressin test with the E.E.G. as a still more sensitive aid to diagnosis is suggested by Blier and Redlich (1947). They tried out the pitressin test on a small group of epileptics with negative E.E.G. records, and on control groups, including 12 "psychogenic fainters." Only 2 of the epileptics had fits, but 9 of them showed E.E.G. abnormalities after the test, compared with only 3 of 21 controls. They believe, therefore, that the method would be useful in distinguishing between epileptic and hysterical or vasodepressor disturbances of consciousness.

Cohn *et al.* (1947) are very sceptical about the pitressin test. They studied the E.E.G. changes associated with water intoxication, brought about by pitressin, in 25 servicemen with a history of syncope or transient impairment of consciousness or fits, and found that low frequency E.E.G. activity results in nearly every case. This type of abnormality differs in no way from that seen in sleep, in insulin hypoglycaemia, and in oxygen poisoning. It is reversible and is not specific for epilepsy, and consequently can never justify an epileptic diagnosis. The uncertainty of producing a clinical convulsion and the non-specific nature of the E.E.G. changes greatly limit the value of the pitressin test. Apparently no paroxysmal outbursts were seen in any of their E.E.G. records.

AETIOLOGICAL FACTORS.—HEREDITY.

Scepticism about the hereditary factor in epilepsy dies hard. Thus, Hartenberg (1946) considers that in the idiopathic complaint it is negligible,

while Marburg and Helfand (1946), in their study of 100 cases of epilepsy attending a nerve clinic, found only 2 cases of parental epilepsy, and very few others showing any suggestion of a familial predisposition. One may be allowed to wonder how thorough was the search.

The importance of heredity, however, was clearly established by Lennox *et al.* (1940) in their classical paper on "The Inheritance of Cerebral Dysrhythmia and of Epilepsy." In 88 families of epileptics, E.E.G. records were obtained from both parents, and in 35 per cent. of them, both records were definitely abnormal, both being unmistakably normal in only 5 per cent. Dysrhythmia was found in more than 60 per cent. of the near relatives of epileptics, being more frequent among the relatives of female than of male patients, and among female relations than among male relations. Twin evidence was added to substantiate the conclusion that dysrhythmia of the epileptic type is inheritable, and represents a predisposition to epilepsy or some allied disorder. Those with this predisposition outnumber epileptics by 25 to 1, and include about 12 per cent. of the whole population. In spite of the difficulties in deciding what degree and kind of E.E.G. abnormality constitute dysrhythmia, the results of this investigation have been widely accepted.

The study of twins has contributed materially to the evaluation of the hereditary factor. Lennox (1947*b*) sums up his work in a recent paper on "Sixty-Six Twin Pairs Affected by Seizures." Forty-three of his twin pairs are monozygotic, and 23 dizygotic, and each group he divides up into those with, and those without, previous brain injury. The 4 classes are then investigated with regard to the presence or absence of (1) seizures, (2) mental decay and (3) cerebral dysrhythmia. With regard to fit incidence, the percentage of twin pairs, in which both co-twins are affected, is monozygotic-genetic (i.e. without brain damage) 83, monozygotic-acquired 16, dizygotic-genetic 6, and dizygotic-acquired 0. Conrad's corresponding figures, 86, 12, 4, 0, are very similar. In co-twins, both with chronic epilepsy, there is close concordance in the age of onset and type of fit, but not in the fit frequency. Intelligence tests show very small differences between the quotients of monozygotic co-twins, unless one has suffered brain damage. Not only is the type of clinical seizure the same in twins, but E.E.G. studies show a transmitted predisposition to particular patterns of brain waves. There is, too, a general correlation between the proportion of individuals with seizures and with dysrhythmia in the 4 groups. Moreover, half the non-epileptic co-twins of monozygotic twins with presumably acquired epilepsy show abnormal rhythms, mostly of the mildly slow type. This is 3 times the frequency of such rhythms in the population generally.

In a further article Lennox (1947*c*) has collected up his work on the genetics of epilepsy. Study of the incidence of epilepsy among 12,000 near relatives of more than 2,000 epileptics, and among twins, together with extensive E.E.G. analyses, has convinced him that a tendency or predisposition to epilepsy is inherited, and not epilepsy *per se*. In speaking of genetic and acquired epilepsy, he recognizes that in most patients both genetic and acquired factors are at work. The incidence of epilepsy is higher among near relatives, if pathology of the brain did not antedate the onset of fits, if the patient's epilepsy

began early in life, if he was mentally abnormal at birth, if he has *petit mal*, or if the patient is a female. The E.E.G. is definitely an hereditary trait, but it must always be remembered that negative E.E.G. findings may not be significant.

A very practical problem arising out of our newer conception of the inheritance factor in epilepsy, is that of marriage and children. Lennox (1945b), in discussing this, estimates that the chance of the child of an "average" epileptic being also epileptic is about 1 in 40. The chance will be less if acquired factors have contributed to the parent's epilepsy, if the family history is clear, if mentality is normal and if the spouse is free of the type of dysrhythmia that suggests predisposition. An E.E.G. record of the prospective spouse, therefore, is likely to be of considerable help to the physician who is called upon to advise. Each case merits careful individual study. In many cases, Lennox holds, the small risk of handing on epilepsy, or a predisposition to epilepsy, to the next generation may be outweighed by the presence of highly desirable physical, mental or spiritual traits in the parents.

SIGNIFICANCE OF EARLY CONVULSIONS.

Peterman (1946) has made a comprehensive survey of convulsions, single or multiple, occurring in childhood. His report covers 2,500 children, seen over a period of 20 years. In 7 per cent. of the cases the first, often the only, convulsion occurred in the first month of life, and in these birth injury was by far the most frequent cause. In 13 per cent., where the first attack took place from the second to the fifth month, acute infection was the commonest cause, with infantile tetany and birth trauma as good seconds. No less than 47 per cent. of the total have their first fit between the ages of 6 months and 3 years, and here, again, acute infection heads the list, with idiopathic epilepsy, birth trauma and tetany well in the running, but some distance behind. Among the remaining 33 per cent., who have the first convulsion between the ages of 3 and 16, the majority are considered to be cases of idiopathic epilepsy. Commenting on these figures, Peterman is inclined to think that acute infections precipitate convulsions only in those children with a predisposition, or low convulsive threshold, and this he has been able to confirm in many cases by the E.E.G. Recurrent convulsions, he holds, are almost always evidence of idiopathic epilepsy. He notes, of course, a large number of less common causes of convulsions in childhood, but failed to find a single case in the whole series in which he could satisfy himself that hypoglycaemia could be established.

The significance of convulsions arising in connection with acute infections, or, as they are often called, febrile convulsions, has been further elucidated by Margaret Lennox (1947). Among 153 cases she finds males twice as common as females. Nearly half the children have a family history of convulsions (not necessarily epilepsy), and two out of every three had their first febrile convulsion between the ages of 1 and 3. In addition, reports are furnished on 52 children whose first attack was a febrile convulsion, but who have since developed epilepsy. In this group the initial convulsions were more severe, and the incidence of birth trauma and of epileptic family history greater. Of the first group of 153, 53 per cent. have normal E.E.G.'s, but 10 per cent.

show definite paroxysmal E.E.G. abnormalities. These have a peak age for the attack, before 1 or after 3, had more severe and frequent fits than the others, and have positive family histories often both on the paternal and maternal sides. Thus, the E.E.G. confirms the clinical picture. As a practical measure, it is suggested that children with febrile convulsions should have an E.E.G. within a week of the attack, a month later, and again at the age of 6 or 7. Anticonvulsant drugs might be usefully administered up to the age of 3.

BIRTH TRAUMA.

The importance of the part played by birth trauma in the causation of epilepsy has been emphasized by Nielsen (1946). He studied the birth sequence in 105 cases of epilepsy, and is satisfied that birth difficulties, probably chiefly asphyxial, are a major cause. Of children whose fits start in the first decade, 60 per cent. are firstborn, and of those whose fits start in the second decade, 51 per cent. Firstborn children are from two to three times as likely to develop epilepsy as are the children of later birth by the same mother. Subsequent investigation (1948) confirms his belief. He has analysed the records of 782 institutional epileptics, coming from families containing 3,275 children in all, or an average of 4.2 children to a family. The ratio of firstborn to later-born children among the epileptics was 1.79 to 1. Discussing how these observations might fit in with the presence of a high percentage of cerebral dysrhythmia among the relatives of epileptics, Nielsen suggests that the dysrhythmia might possibly be due to asphyxia of insufficient degree to produce epilepsy, or that it may be dystocia which runs in families, epilepsy being only a sequel to dystocia.

LATER TRAUMA.

War experience forms the basis of many articles on traumatic epilepsy in adult life. Watson (1947) discusses the incidence of late epilepsy following cranio-cerebral injury in the war. Of 279 cases, 36 per cent. developed fits during the first two years, mostly between the fourth and eleventh month after injury. The area incidence was frontal 27 per cent. central 51 per cent., occipital 33 per cent., and temporal 35 per cent. Sixty-two per cent. had generalized convulsions, but in one-third of these there was some focal manifestation; 26 per cent. exhibited only focal symptoms; 8 per cent. had visual seizures; 29 per cent. had Jacksonian motor seizures; 4 per cent. Jacksonian sensory marches; 2 per cent. olfactory seizures; and 8 per cent. psychic equivalents. He found no evidence that an inherited predisposition played any part in determining the onset of traumatic epilepsy. The mortality during the 2-year follow-up period was 4 per cent.

Quadfasel and Walker (1947) present a series of 246 cases of penetrating wounds of the head, with neurological, E.E.G., radiological, psychological and therapeutic findings. They find patients with infected penetrating wounds in the parietal region most prone to develop fits. Although the attacks in these traumatic cases were focal in origin, many of them are clinically indistinguishable from idiopathic fits. Anticonvulsant drugs are very often effective. In drug-resistant cases, the epileptogenic focus identified by E.E.G.

records and confirmed by direct electrical stimulation, was removed surgically. Rehabilitation by vocational guidance is described.

The anatomy of traumatic epilepsy has been studied by Ritchie Russell (1947), who devised a new method for more accurate localization of the site of injury. He compares the site of injury of 138 cases who developed fits with that of 222 cases not followed, up to 18 months or 2 years, by epilepsy, and finds that in the former group the sites tend to accumulate in certain areas. He discusses the possibility that injury to "suppressor" areas may play a part in causing traumatic epilepsy.

Early and late traumatic epilepsies are considered to be aetiologically distinct, and Whitty (1947) has attempted to assess the significance of the former. In a large series of brain injuries, he found that 6.7 per cent. experienced fits within the first few days. This figure is almost certainly too small, as some patients will have had unrecorded fits immediately after the trauma. In these early cases, site of injury influences the type of attack, but not the incidence of fits. The extent of surface damage is important, and constitutional factors often play a major part. Follow-up studies show that over half the cases become the subjects of late traumatic epilepsy. This represents an incidence 3 times as great as that expected from the whole group of gunshot wounds of the brain. Whitty believes that in late epilepsy, trauma site may play a more important, and constitutional factors a less important, part than in early cases.

The incidence and significance of E.E.G. abnormalities in traumatic epilepsy, both early and late, have been studied by Denis Williams (1944). Comparison of the E.E.G. in a group of 241 normal, healthy controls, 234 patients with head injury without epilepsy, 210 patients with traumatic epilepsy, 275 patients with apparently idiopathic epilepsy, and 42 patients who were examined by E.E.G. before and after the onset of traumatic epilepsy, shows that 9 per cent. of the traumatic epileptics and 27 per cent. of the idiopathics show larval, or characteristic epileptic outbursts. Transient disturbances in the E.E.G. occur in less than 1 per cent. of normal subjects, in 14 per cent. of uncomplicated head injuries, in 25 per cent. of traumatic epileptics, and in nearly 60 per cent. of idiopathic epileptics. Paroxysmal outbursts are much more frequently found in patients with penetrating head injuries than in a similar group with closed injuries. The type of E.E.G. abnormalities recorded in the traumatic epileptics before and after the onset of seizures are similar to those recorded in the group of non-traumatic epileptics. It is most common for the E.E.G. to remain unchanged in any particular.

Immediately after the head injury it is usual to find gross abnormalities, characteristic of severe cerebral damage, which in a few weeks subside, with the gradual reappearance of a normal rhythm. During this period of recovery, another kind of abnormality is established, which steadily increases until it becomes first an indefinite dysrhythmia, later a more definite larval outburst, then, finally, frank epileptic fits. These changes are indefinitely related to the time of the injury, and to the time of onset of the seizures, and bear no relationship to the injury in morphological characteristics, voltage, period, distribution and number. They may arise from points in the hemisphere

remote from the damage area, and although the primary or direct effects of injury are usually reversible and transient, these secondary changes are irreversible and permanent.

When changes, which have been described as larval or characteristic epileptic outbursts are seen at an interval after injury, epilepsy is virtually certain to supervene. When less distinct paroxysmal discharges occur, there is an even chance of traumatic epilepsy, but in all other cases the E.E.G. is no guide as to the probability of epilepsy following cerebral injury. (Review in *Epilepsia*, 1946.)

REFLEX EPILEPSY.

Reflex epilepsy is a term that should only be used when the fit occurs in response to a highly specific stimulus; even so, the reflex may be a conditioned one. Sensory precipitation of fits, a less misleading term, is not very uncommon.

Shaw and Hill (1947) have made a thorough and illuminating study of an unusual case of musicogenic epilepsy. The patient was a woman who had a psychomotor attack, with corresponding E.E.G. accompaniment, whenever she heard music. Emotional change preceded the fit, but Shaw and Hill show conclusively that the fit was not, in their case, determined by respiratory or cardiovascular changes. The cortical discharge, indeed, as shown by the E.E.G., did not appear for 6 or 7 seconds after the clinical onset. The fit pattern, optokinetic response and inter-fit E.E.G. records pointed to an epileptogenic area in the left temporal lobe. The authors discuss the relation of their case to other observations on audiogenic fits, including those in rats, and the possible methods of fit production.

Cases are on record in which there is an association between epileptic response and peripheral injury. Parsons-Smith (1948) reviews these, and describes that of a man with an injury of the left hand. Neither the actual nerve injury, nor ordinary pain, pressure or touch stimuli, but only a light tickling touch applied to the area supplied by the injured nerve acted as excitant in this case. In response to this highly specific stimulus, focal attacks made their appearance within 24 hours of the injury, and continued for several months, on two occasions progressing to major fits with convulsions.

The inception of clonic movements in the exact area of stimulation is remarkable. A study of the article leads one to wonder what part an existing cerebral cysticercosis may have played in facilitating the response.

PETIT MAL.—DEFINITION.

Classification and nomenclature of fit types has always been unsatisfactory. In general practice, two types are usually recognized, major and minor. The former denotes generalized convulsions with tonic-clonic sequence. The latter covers every other type of epileptic attack. It is probably better now to drop the word "minor" altogether, and to speak of fits of the major type (complete or incomplete), psychomotor attacks and *petit mal*. Lennox (1945a) groups together 3 types of attack which, in his view, should be included under the term *petit mal*. These three—true *petit mal* or pyknolepsy, myoclonus and akinetic

epilepsy—he calls the *petit mal* triad. The grouping was first made on E.E.G. similarities, for these conditions are all associated with alternate spike- and slow-wave activity, but they have many other characteristics in common. Thus, they are all predominantly childhood seizures, tending to disappear in adult life, they are usually very frequent, brief, abrupt in start and finish, sensitive to change in acid-base balance, or oxygen or sugar content of the blood, resistant to the usual anticonvulsant drugs, but controlled by tridione. Moreover, except in some akinetic cases, there is no evidence of cerebral pathology, and the patient's mentality is well maintained. The delimitation of this *petit mal* triad is of more than theoretical interest; it is essential for the right choice of medication.

PETIT MAL.—LOCALIZATION.

Penfield and Jasper (1947) consider that *petit mal* attacks characterized only by loss of consciousness, can be called highest-level seizures, and they predicate the existence of a mass of grey matter ultimately connected with the maintenance of consciousness. The fact that when movement is added during the attacks it is universal, or at least bilateral, suggests anatomical connections with both hemispheres. Minor attacks, due to limited discharge in cortical areas other than frontal, do not show initial loss of consciousness; in these areas the units are intermediate stations between spinal levels and the highest level. True, seizures arising from the anterior portions of the frontal lobe are characterized by initial loss of consciousness, but the removal of the lobes does not arrest consciousness. Injury to portions of the diencephalon may, however, produce unconsciousness with little evidence of paralysis of cortical function. The authors postulate, therefore, a highest-level centre in the diencephalon with direct connection with the anterior portions of the frontal lobes, and ready access to widespread cortical areas in both hemispheres. This centre is the origin of, or the integrating centre for, highest-level seizures, and is situated, contrary to traditional opinion, in an older subcortical zone.

Jasper and Droogleever-Fortuyn (1947) carry the localizing process a stage further. All the E.E.G. characteristics of *petit mal* epilepsy are produced by rhythmic electrical stimulation of a small area of the medial intralaminar region of the thalamus in cats, and they suggest that this area is capable of synchronizing the rhythmic activity of various semi-independent systems into a rhythmic beating of all the thalamo-cortical systems. If this is so, no generalized cortical disease need be postulated to explain the generalized cortical discharge of *petit mal*.

EQUIVALENTS.

The idea that recurrent attacks of dizziness or headache, of outbursts of anger or cruelty, or even of paroxysmal abdominal pain should often be regarded as epileptic equivalents, is not a new one, and it has recently received fresh support from Waggoner and Bagchi (1947), who studied 21 patients showing one or more of these symptoms, and most of whom had other evidence of psychoneurosis in addition. E.E.G.'s generally showed definite dysrhythmia, and treatment by anticonvulsant drugs combined with psychotherapy was

effective. Proctor (1947) would also include under the epileptic syndrome many less-defined periodic manifestations, involving in most cases some impairment of consciousness. Thus, he cites cranialgia, emotional instability, vasomotor instability, periods of impaired or lost consciousness, and personality disorders, any, or all, of which may or may not be associated with epileptic fits. These manifestations, he finds, are readily controlled by phenytoin, but show little response to phenobarbitone. They have a common E.E.G. component, namely, half and double alpha variants. He considers that the recognition of such a syndrome enlarges our conception of epilepsy. Pugh (1947), in seeking to define epileptic equivalents, finds that they are characterized by bizarre motor activity, by hallucinations or illusions, or by acute manifestations involving the autonomic nervous system. There is amnesia, but no loss of consciousness. On these criteria, 1 per cent. of 5,000 convulsive cases experience equivalents, and these Pugh divides into motor, sensory and autonomic, differentiating them carefully from psychotic states and behaviour disorders. In 36 per cent. the manifestations were motor, and here the E.E.G. gave confirmatory evidence in 75 per cent.; in 48 per cent. they were sensory, with 91 per cent. positive E.E.G.'s (amnesia in these cases could obviously not have been complete—it is called "relative"); in 10 per cent. they were autonomic, with 71 per cent. positive E.E.G.'s. In the latter group, amnesia was not consistently present, and the evidence of sympathetic or parasympathetic overactivity was located in the vasomotor, cardio-respiratory, diaphoretic or gastro-intestinal systems. Treatment of the equivalents was not often effective.

EQUIVALENTS.—ABDOMINAL PAIN.

Periodic attacks of abdominal pain have long been recognized as possible epileptic manifestations, and indeed the frequent occurrence of an isolated epigastric aura is suggestive. Moore (1945) has made a careful investigation and report of 6 cases in which paroxysmal abdominal pain was either the only, or the dominant, symptom of an epilepsy whose diagnosis was established by the symptomatology, the E.E.G. findings and the response to anti-convulsant drugs. Five of the 6 cases had, as a matter of fact, evidence of organic cerebral disease or damage. Moore is inclined to think that the phenomenon is not very uncommon, and suggests 6 criteria for diagnosis: (1) exclusion of visceral disease, (2) adequate history, (3) attack pattern of epileptic order, (4) associated epileptic phenomena, either preceding or during the attack, (5) objective evidence of cerebral disease or dysfunction, and (6) effect of anticonvulsant drugs on the attacks of pain and on the E.E.G.

EQUIVALENTS.—LAUGHTER.

Paroxysmal compulsive laughter, as an epileptic variant, is considered at length by Roubicek (1946). Of 5 cases studied, 3 had *petit mal* or major fits as well as the laughter attacks. Hyperpnoea accompanying the laughter may have been a factor in precipitating some of these fits. The thesis that the laughter arises in the midbrain and thalamus is advanced. Anticonvulsants are only found to be effective when both laughing attacks and fits are present.

EQUIVALENTS.—NYMPHOMANIA.

Short paroxysmal attacks of nymphomania in a woman of 43 are reported by Erickson (1945). After 2 years the attacks served to usher in typical Jacksonian seizures, spreading first to the left lower extremity and followed ultimately by post-ictal paralysis. A neoplasm was found irritating the cortical area in the right paracentral lobule, which represents the topical projection of the genital structures. The neoplasm was removed, and the attacks ceased.

PSYCHICAL SEIZURES.

In discussing psychical seizures and the psychical elements in motor and sensory seizures, especially those of focal origin, Penfield (1947) refers first to the unconsciousness, which is the dominant characteristic of the contraversive attack resulting from damage to one frontal pole. Attacks of perceptual illusion arise from a focus in one temporal pole. The patient experiences a sense of things going away or coming nearer, of familiarity or *déjà vu*, or of a strangeness or unreality in the environment. Hallucinatory seizures are usually visual or auditory and may be simple or complex in nature. They are recognized by the patient as unreal, and again rise from a focus in one temporal lobe. What may be described as forced thinking has been experienced by a few patients with an epileptogenic focus in the posterior part of one frontal lobe, in front of the motor cortex. It is regarded by the patient as a fit warning. Four cases are quoted of stereotyped behaviour occurring in patients with epileptogenic foci in the median or posterior part of one frontal lobe near the longitudinal fissure. In one case the abnormal E.E.G. discharge started over $2\frac{1}{2}$ minutes before the first somatic evidence of a brief contraversive attack, and long outlasted it. Stereotyped behaviour and confusion in these cases often appeared to be both ictal and post-ictal. They may be evidence of local paralysis arising either during or immediately after the fit, or they may be due to the discharge of some neuron pattern. Post-fit automatism is a common sequel to attacks arising from different areas, but is most often seen after short fits arising in the region of the Sylvian fissure, when it tends to take a masticatory form with a period of purposeless movement and amnesia. In these cases it is clear that the highest centres, providing the anatomical substratum for conscious activity, are out of action. Automatic activity, constituting an attack (ictal automatism), most often occurs in idiopathic cases, and is evidently due to a discharge at this highest level of integration which, Penfield thinks, is in a midline area in close anatomical relationship to the frontal lobes. Finally, Penfield refers to prolonged psychotic states which may follow a series of fits or status epilepticus. In all such cases where a focal discharge could be proven, the location was in one or other frontal lobe.

Advances into the broad field of neurobiology by psychiatrists and neurosurgeons will provide opportunities for perceiving cerebral mechanisms that are the essential accompaniments of changing states of mind and spirit.

MENTAL ACCOMPANIMENTS.—INTELLIGENCE.

Collins and Lennox (1947) assessed the intelligence of 300 private patients, 100 children and 200 adults. They estimate that this class of patient constitutes 62 per cent. of the epileptics under medical treatment in Massachusetts, and represent of course, an educational, economic and occupational standard above the average of the general population. The range of I.Q. was from 47 to 153, with an average of 109. The most notable observation is that acquired epilepsies (defined as those with a history of severe head injury, focal seizures, a focal form of seizure discharge in the E.E.G., or neurological signs of brain damage) come off worse, with an average of I.Q. 10 points lower than genetic epilepsies.

The percentage of epileptics with I.Q.'s over 100 in the following 4 groups is illuminating: epileptic colony 4, out-patient clinic 14, private patient with damaged brain 60, private patient with undamaged brain 79. Among their private patients Collins and Lennox find that early age of onset is prejudicial to intelligence, but not, be it noted, a long history of fits. With regard to clinical type, pure *petit mal* is the most favourable, and a combination of major fits and psychomotor attacks the least. E.E.G. correlation is shown by highest scores for those with normal records or only *petit mal* discharges, and lowest scores for those with very slow waves or *petit mal* variants. Verbalized and block-design tests are performed best, while rote memory and concentration come off worst. Pattern analyses resemble the normal more closely than they do the psychotic or neurotic.

Sands and Price (1947) have made a somewhat similar investigation on 77 adult patients discharged from the New York Neurological Institute. They used the pattern analysis of the Wechsler-Bellevue Intelligence Scale with its subtests of various mental functions. They grouped their cases into: (1) idiopathic epilepsy without personality problems, (2) idiopathic epilepsy with personality or adjustment problems, and (3) organic (symptomatic) epilepsy, establishing in each case a normal control group from the general population norms set up by Wechsler. They find that the first 2 groups are in close agreement with each other, and with the general population. The I.Q.'s are within normal limits, and no psychometric signs or patterns pathognomic of epilepsy can be established. In the symptomatic group, on the other hand, the I. Q.'s are about 11 points lower than among idiopathics, and this group failed markedly in the digit span and digit symbol subtests.

So far as intelligence is concerned, the impression left by these two pictures is an unduly encouraging one. Sheps (1947) assessed the intelligence of 370 male non-institutionalized epileptics of military age, and found that the average intelligence was significantly lower than that of the general population.

Bridge (1947), in a follow-up study of a large group of epileptic children, who had attended a hospital clinic, finds that 65 per cent. of them are suffering from mental retardation of a degree sufficient to constitute a social handicap, a social handicap which he defines as serious in the majority of those who possess it.

This diversity in the estimated intelligence of epileptics shows how necessary it is to define, as exactly as possible, the group of epileptics upon whom any

given observations and statistics are to be based. The whole field of epileptic research is sadly marred, and the emergence of truth delayed, by failure to make this definition. It would be easy to produce whole series of seemingly quite incompatible facts and figures worked out by competent observers in clinical, psychological, social and even more strictly scientific and laboratory work on epilepsy. In most cases careful delimitation of the group concerned would explain the discrepancies. This is no mere subdivision of epileptics into institutional and non-institutional. Something much more detailed and thorough should be set out in every article published. Some institutions cater primarily for the insane, some for the mentally defective, some will only admit really intelligent epileptic children, some are filled chiefly by the chronic and deteriorated type. Definition of an institutional group must include some account of the types of case which the institutional authorities are willing to admit, or make a practise of excluding. Outside institutions, the group of epileptics attending the out-patient clinic of a neurosurgeon will differ from those at a neurological clinic, a psychiatric out-patient department, a child-guidance session, a general practitioner's surgery or a central Labour Exchange. The reason for attendance constitutes a specific selective factor, and will modify the survey results of the group in almost any field of research.

DETERIORATION.

Mental deterioration has long been believed to be the lot of most epileptics, and in the past many investigators have sought to correlate it with the frequency and severity of fits. The general conclusion that a high incidence of major fits is the important factor in deterioration must be accepted, with the proviso that severe deterioration occasionally occurs with a low fit incidence, and that some writers consider very frequent *petit mal* to be even more prejudicial than the more severe attacks. Earlier work was mostly carried out on institutional patients, but a recent search for deterioration in this class produced rather surprising evidence of its absence. Falk *et al.* (1945) tested and retested 85 cases with the Stanford-Binet tests three or four times, over periods varying from 9 to 14 years. The age range of the patients was from 23 to 63, and the I.Q. range from 25 to 103, the majority being fairly low down in the scale. No evidence of deterioration was found, either in the idiopathic or the organic group, but there was a significant drop in the I.Q. in 3 cases in which the epilepsy was associated with psychosis.

Mayman and Rapaport (1948) survey a wide field for evidence of mental deterioration, and, though they conclude that such deterioration is not characteristic of convulsive disorders, the incidence is, in their view, probably as high as from 6.5 to 13 per cent. of all non-institutional cases, even after patients with primary mental defect have been carefully weeded out. The evidence that duration of the complaint, the fit frequency or severity, or the use of drugs play much part in the production of deterioration they consider inadequate. Its association with brain damage rests on firmer ground. The authors are inclined to think that there may be a specific type of deterioration, as described by MacCurdy many years ago.

In a study of the intelligence of 186 co-twins, 30 of whom had had epilepsy, Lennox and Collins (1945) adduce strong evidence to suggest that, with good mental inheritance, intelligence can be sustained in spite of fits, provided there is no acquired gross pathology of the brain.

THE PSYCHOGENIC FACTOR.

The belief that many, or even most, cases of epilepsy are psychogenic in origin still has its adherents. Aring *et al.* (1947) cite 3 cases of idiopathic epilepsy which illustrate the intensive charge of affect caused by emotional conflict, and subsequently discharged by the neuronal explosion of a fit. The emotional conflict long antedated the onset of attacks, and continued to act as fit precipitant. Psychotherapy played an essential part in successful treatment. The authors consider that this interpretation of the role of emotion obviates the necessity for a concept of an epileptic personality, or for the symbolic interpretation of the fit.

A somewhat similar interpretation of epilepsy is reached by Fuchs (1947), after making an intensive study of 25 epileptic children. He finds the fit to be a symptom of deep-seated conflict, in which the child has been able to discharge his embittered feelings and emotional strain. Epileptic children are not emotionally impoverished, rather the reverse, being as a class nervous and unusually responsive to environment. Such response manifests itself not only in terms of happiness or unhappiness, but also in terms of fits. The author cites at length numerous case-histories illustrating emotional conflict and the psychogenic nature of the disorder. He does not believe in a distinctive epileptic type of personality.

If it is true that epileptics are rather more labile emotionally than others, it is a curious fact that acute emotional stress, engendered by air raids and air-raid alarms, has no effect on the fit incidence or the mental outlook. This was the experience of Fox (1941), who had ample opportunity of observing nearly 500 institutional cases, more than half of them children, under prolonged stress of this type, and was confirmed by Shafar (1941) from fit statistics and psychological observation of a large group of out-patients in the London area. The origin of the disorder in the first instance may be psychological in some cases, but these observations go a long way to discount acute mental stress or conflict as a fit precipitant in established epilepsy.

RORSCHACH TEST.

Kogan (1947) matched, for age and intelligence, 10 children with idiopathic epilepsy with 10 non-epileptic children from a child-guidance clinic for intensive psychological tests, especially the Rorschach test. Psychological tests revealed no gross similarities of test patterns or scores in the epileptic group, nor did the Rorschach test show statistically significant differences between the two groups. It is concluded that the Rorschach test is a measure of personality disturbance, independent of epilepsy, in the composite factors of which, however, seizures may play a minor role. The reaction of the epileptic to his epilepsy and to his environment are neither unique nor irreversible.

SUGGESTIBILITY.

The common belief that suggestibility and persistence are characteristics of epileptics has been investigated by Brady (1948). Using the Body Sway test for suggestibility, and only a simple motor test for persistence, she compared 200 epileptics with a similar number of mental defectives, and with scores found by others on normal and neurotic subjects. She finds that neither mental defectives nor epileptics are more suggestible than the normal group, but they are both significantly less suggestible than neurotics. They show, however, a much higher degree of persistence.

OBSESSIONS.

The association of obsessional and compulsive states with organic disease has often been pointed out. Various reports have been made of epileptics who manifested periods of obsessional doubt, compulsive laughter, and so on, and E.E.G. studies of patients with obsessions (Pacella, 1944) at least suggest the possibility of an epileptic basis in some cases. Garmany (1947) reviews the evidence for such an association, and recounts the history of an epileptic who, after his fits had stopped, developed a severe obsessional state in middle life. He thinks it possible that a single pathology may be responsible for both conditions, and that from some affected extrapyramidal area a discharge may spread to both hemispheres, producing a generalized seizure. He reminds us that it is now established that generalized fits can arise from subcortical disease, and that obsessional states can undoubtedly occur in connection with ascertained disease in the upper part of the brain stem.

HISTOLOGY.

In the course of 15 post-mortem examinations of cases of chronic epilepsy, Scheinker (1947) found extreme venous distension in circumscribed areas of white matter. These, he thinks, may be due to prolonged and repeated vasomotor changes, and are definitely not evidences of vascular malformation. The wider areas of atrophic sclerosis in post-traumatic epilepsy he regards similarly as evidence of prolonged circulatory disturbances.

BIOCHEMISTRY.

Biochemical changes occurring during seizures are discussed by Colfer (1947), who finds that experimental convulsions in animals, studied by micro-crystallography and micro-incineration, consistently show a redistribution of cortical electrolytes with gain of sodium and loss of potassium, a redistribution which he attributes to changes in permeability. Further *in vitro* studies show that an increased pH produces intraneuronal changes similar to those seen with induced convulsions, while a diminished pH has the opposite effect, all the changes being reversible. Desoxycorticosterone acetate in rats inhibits audiogenic convulsions, as also does a low potassium diet.

Stone *et al.* (1945) find that cerebral lactic acid increases during the convulsive electric discharge produced by metrazol in an animal immobilized with dihydro-beta-erythroidine and maintained by artificial respiration. A decrease

in cerebral phosphocreatine usually occurs, with a corresponding increase in inorganic phosphates. The observed chemical changes occur in the absence of any decrease in the cerebral oxygen supply, and are interpreted as indicating that the oxidative processes lag behind an increased energy expenditure during convulsive activity. Other detailed researches into cerebral metabolism during induced convulsions in animals have been carried out by Gurdjian *et al.* (1947), and by Davies and Rémond (1947), and histochemical studies, controlled by E.E.G. recordings, have been made on epileptogenic areas in man and in monkeys (Pope *et al.*, 1947).

Gibbs *et al.* (1947) measured the minute-volume blood flow through the human brain by puncturing the internal carotid artery and internal jugular vein through the unbroken skin. This rather daring procedure was carried out on 6 non-epileptics and on 6 epileptics during inter-fit periods. The results in the two groups showed no difference, either in the rate of flow or in the arterio-venous differences in oxygen, sugar or carbon-dioxide content. They confirmed their previous findings (1935), that breathing a high carbon-dioxide mixture doubles the cerebral blood flow, whereas lowering the carbon-dioxide content, as by hyperventilation, can reduce it by a half. Unfortunately, they were not able to furnish any records obtained during an attack.

A new approach to the biochemistry of epilepsy has recently been made by Eeg-Olofsson (1948), who has measured the total protein, globulin and albumin in the lumbar fluid of 133 epileptics and 67 controls. He finds that two groups can be sorted out from the rest of the epileptic material, those with high total protein and those with low globulin/albumin quotients. A careful scrutiny of the clinical evidence shows that where high total protein has been repeatedly demonstrated, it is probable that an intracranial process of some kind exists, and for these cases the author proposes the term "epilepsia hyperproteinorrhachia." It is worth noting that he finds no correlation between the occurrence of E.E.G. foci and increased total protein. Abnormally low globulin/albumin quotients are often found in epileptics, but not in the controls, and the author believes that the investigation of the protein fractions may lead to an understanding of the deeper nature of the epileptic syndrome. Protein changes are not influenced by the time relation to the previous attack, to the fit frequency or to the duration of the disease.

EPILEPSY AND ALLIED CONDITIONS.—CEREBRAL TUMOUR.

Hoefer *et al.* (1947) found fits of some kind occurring in 34 per cent. of a series of 506 hemisphere tumours, including brain abscesses and subdural haematomas. The cases are considered under the headings of the type of tumour, location of tumour, the type, onset and duration of fits, and the E.E.G. findings. The conclusions in general confirm those recorded in Penfield and Erickson's book (1941). Fits are more prevalent and more likely to be the first symptom in slow-growing tumours. Generalized E.E.G. changes, similar to those seen in epilepsy, are rare, and significant response to overventilation rarer still, though both abnormalities are commoner than in the population generally. The authors conclude that a predisposition to epilepsy is not a major factor in the production of attacks in cases of brain tumour.

ANAESTHETIC CONVULSIONS.

The literature of anaesthetic convulsions, or ether convulsions as they are wrongly called, is voluminous, and various physical conditions and chemical agents have been incriminated. With the aid of the E.E.G., Williams and Sweet (1944) have made it clear that up to date the main point has been missed. Out of 22 patients who had had anaesthetic convulsions, three-quarters showed persisting E.E.G. abnormalities, in no way distinguishable from those seen in epilepsy. Nor were the fits, in 42 cases, different clinically from epileptic fits. It is reasonable to assume, therefore, that the convulsions are evidence of an inherited predisposition, and that some of the other factors suggested may act as weak precipitants of fits. Such is almost certainly the part played by the anaesthetics themselves, which are weak convulsants in varying degree. Thus, chloroform is probably least effective, while vinesthene, as shown by Dawkins (1940), is more convulsant than most. It would seem that preliminary E.E.G. examinations, followed, where indicated, by anticonvulsant drugs, should go far to prevent the occurrence of convulsions under anaesthesia.

ECLAMPSIA.

The position with regard to eclampsia has been elucidated along similar lines by Rosenbaum and Maltby (1943). Twenty patients with eclampsia were compared with a similar number of patients showing non-convulsive toxæmias of pregnancy. The incidence of a family or personal history of fits was 60 per cent. in the first group, 10 per cent. in the second; E.E.G. abnormalities suggesting cerebral dysrhythmia were 65 per cent. in the first group, 10 per cent. in the second. The associated toxæmia, therefore, is regarded as a trigger mechanism releasing overt manifestations of a pre-existent dysrhythmia. An E.E.G. in toxæmias of pregnancy would, in appropriate cases, suggest anticonvulsant medication to obviate the development of fits.

FAINTING.

An unwillingness to try to differentiate between syncope and epilepsy (or the convulsive tendency) is shown in an article by Moloney *et al.* (1946) on "Syncope in Blood Donors." In over 16,000 donors, one in 100 showed severe syncope, one symptom of which, in 28 per cent. of the cases, was said to be generalized convulsions. (In this country, the Medical Research Council Report (1944) records the appearance of convulsions in only 7 per cent. of fainters among blood donors.) In these 28 per cent., and probably in others, it is surely reasonable to suppose that the syncope was facilitated by a pre-existing convulsive tendency, which should be manifest on an E.E.G. record. That this is so is suggested by the work of Redlich (1946), who used the E.E.G. in the investigation of a large group of patients at an Army Neurological Centre. The clinical diagnosis was epilepsy in 95 cases, fainting in 29, hysteria in 10 and doubtful in 61. In all patients with a clinically certain diagnosis the E.E.G. was confirmatory in 61 per cent., intermediate but consistent in 24 per cent., and non-confirmatory in 15 per cent. In the 61 patients where

the clinical picture gave rise to doubt, the E.E.G. was of material help in determining a diagnosis of epilepsy in 12, and of syncope in 26. Differentiation between epilepsy and fainting is often extremely difficult, and it is encouraging to find that the E.E.G. is able to assist in 2 out of 3 doubtful cases, but as Redlich points out, we must not allow E.E.G. findings to override clinical judgment.

BREATH-HOLDING SPELLS.

Breath-holding spells are not very uncommon in the first year or two of life. They are brought on by anger or frustration, less commonly by pain or fear, and usually disappear by the end of the third year. Bridge *et al.* (1943), in a considerable account of these attacks, record that sometimes they are more severe and may go on to cyanosis, unconsciousness and epileptiform convulsions. The onset in response to frustration, and the orderly sequence of crying, apnoea and then convulsions, will usually make the diagnosis pretty clear, and the E.E.G., say the authors, will often help. Rarely, the condition may be seen in infants who have already had epilepsy, or the epileptiform attacks may outlast the early years and merge into chronic epilepsy. The authors adduce evidence to show that, on the one hand, the more severe breath-holding spells may be found in children with a predisposition to epilepsy, and that, on the other hand, the spells themselves may, in certain cases, play a dominant part in the inception of a chronic epilepsy.

CYSTICERCOSIS.

In a comprehensive paper on cysticercosis, Dixon and Hargreaves (1944) confirm and extend McArthur's classical observations. In a study of 284 cases, 274 of whom were infected in India, they find that the epileptiform manifestations show great variety. Localized paraesthesias, transient monoplegias, aphasias and amnesias may occur with or without typical Jacksonian attacks or major fits, and there may be changes in personality or disorders of behaviour. In diagnosis a negative x-ray is not final, and the history is of first-class importance. Surgery, in the few cases in which it has been tried, has been uniformly unsuccessful, as the cysts are almost always multiple. The prognosis, even in respect of the fits, is a good deal more hopeful than is generally supposed.

Obrador (1948) attempts to classify cases of cerebral cysticercosis according to their site, into cortical, ventricular, basilar and diffuse, and outlines the clinical picture appropriate to each group. He emphasizes the need to bear the condition in mind when, in a young person, there is a long history of variable symptoms with an irregular and diverse neurological picture of a progressive nature. He attaches great importance to the examination of the cerebro-spinal fluid. This may show non-specific features suggestive of inflammatory trouble, together with eosinophilia and a low sugar content, and also, much more important, a specific reaction to the complement fixation test with a specific antigen.

CANINE HYSTERIA.

That a syndrome of epileptiform convulsions, irregular motor activity and anxiety is commonly seen in dogs, and is associated with a wide variety of aetiological factors, has been known for a long time. Two years ago, Mellanby (1946) showed that the syndrome was related to the effect that the agene process had on wheat flour. As we have been eating agenized flour for a quarter of a century, the question arises whether any deleterious effects have accrued to the human gastrointestinal tract or the human nervous system, and, further, whether a study of canine hysteria may throw light on the problem of epilepsy or of abnormal behaviour in men. Silver *et al.* (1947) report that dogs fed on an otherwise adequate diet containing 75 per cent. agenized flour develop epileptic fits with typical E.E.G. abnormality. Newell *et al.* (1947) confirmed these observations and proceeded to feed 5 healthy children with daily diets including 70–105 gm. of wheat products treated with 3–20 gm. of nitrogen trichloride (agene) per hundredweight, more than enough to cause severe symptoms in dogs. No clinical changes were observed, nor did E.E.G. recordings, during the 2–4-week period of administration, show any change. This is reassuring, but does not exclude the possibility of deleterious effects, epileptogenic or other, that might arise from sustained intake of smaller quantities. Parry (1948), reviewing the present position, points out that while the primary hysterogenic factor is a noxious chemical agent produced, or whose action is enhanced, by agenizing wheat flour, the onset of attacks may be in part due to the interplay of other factors, whether neuropsychological, dietetic or metabolic. There is a field here for further team work by biochemists and electrophysiologists.

HYPOGLYCAEMIA

Hoefel *et al.* (1946) describe the neurological and psychomotor manifestations observed in 27 patients with verified adenoma of the islet cell apparatus of the pancreas. All the patients showed manifestations of this type, usually clearly associated with the fasting state, and covering a very wide field. Lightheadedness, sweating, tremors, inco-ordination, paraesthesiae and diplopia were among the most common. Some psychomotor symptoms were noted in every case. These took the form of confusional states, dullness, noisy behaviour, incoherence, and so on. Major epileptic fits were seen in 5 cases, but in most of the others attacks suggestive of epilepsy—coma, fainting, muscle twitching, staring turns like *petit mal*, involuntary movements, clonic or irregular—were noted. The authors' findings differ in some respects from those of therapeutic insulin shock, and possible reasons for this difference are considered. E.E.G. records were typical of depressed cerebral metabolism, but, in addition, convulsive patterns, such as spike and wave outbursts, were common, even among patients who had had no convulsive seizures.

CONVULSANT THERAPY.

Since the institution of convulsant therapy, whether chemical or electrical, occasional instances of spontaneous fits occurring subsequent to treatment have been recorded. The important question arises as to whether, in these

cases, there was a pre-existing predisposition to convulsions, or whether the spontaneous fits must be wholly attributed to the therapy. Pacella and Barrera (1945) found among more than 500 patients who received E.C.T., two who had spontaneous generalized fits, $6\frac{1}{2}$ to 8 weeks after termination of the treatment. The family history was clear in both cases, nor had either patient had fits previously. E.E.G. records had, however, been taken prior to treatment, and both showed abnormalities suggestive of a convulsive tendency. It appears, therefore, that these spontaneous fits are overt manifestations of a pre-existing predisposition, and that a pre-shock E.E.G. record is called for, especially in patients with a family or personal history of convulsions. Taylor and Pacella (1948) take the problem a stage further by discussing whether abnormal E.E.G.'s in patients about to receive E.C.T. constitute an undue risk. They note that in over 1,000 patients with normal pre-treatment records, not one developed spontaneous fits. Among 56 patients with previously abnormal E.E.G.'s, who received E.C.T., only 2 had spontaneous fits afterwards, but these, in one case, continued for 3 years. Four patients with a history of epileptiform seizures, maintained on anticonvulsant medication during treatment, had no subsequent increase of fits. In only 6 cases did the E.E.G. retain the slow wave activity characteristically following E.C.T. for significantly longer periods than in patients with normal E.E.G.'s. The authors conclude that, unless a focal or expanding lesion is suspected, E.C.T. is not contra-indicated for these patients.

WITHDRAWAL OF BARBITURATES.

An interesting phenomenon, which must be fitted into any explanation of the mode and site of action of barbiturates on the central nervous system, is the occasional occurrence of a convulsive seizure following barbiturate withdrawal. Osgood (1944) cites 9 cases of this type, none of whom had had fits previously, and in no case did the fits persist.

CRIME.

A note on the importance of the E.E.G. in determining whether an offender did not know what he was doing at the time of committing the offence is made by Sessions Hodge (1948). He reviews the records of 140 persons referred for examination in connection with anti-social acts. In 26.2 per cent, there was an abnormal E.E.G. Included in this number were 3 groups. In the first group (7.8 per cent. of the total) there was a clinical history of major or minor fits; in the second (4.2 per cent.) there was clouding, diminution or loss of consciousness under hyperpnoea, preceded by the appearance of a complex of high-voltage waves at 1.5 cycles per second in the E.E.G. In the third group (14.2 per cent.) there was no clinical history of fits, nor clouding of consciousness under fasting and/or hyperpnoea, but there were E.E.G. abnormalities of a definite type. All these subjects, then, were liable to episodic disturbances of cortical function, which may have interfered with cortical integration, and it may well be that at any given time they were unable to appreciate fully the nature of their own actions.

EPILEPSY AND PREGNANCY.

The relation between epilepsy and pregnancy has been well reviewed by Burnett (1946). It is generally agreed that epilepsy has no effect upon pregnancy, but the effect of pregnancy on epilepsy varies greatly and appears to be quite unpredictable. The fits may be reduced, or increased, or remain unaffected. No statistical agreement can be found between different observers, but Burnett believes that the cases divide themselves fairly evenly into the 3 classes. Patients whose fits tended to occur at menstrual periods do not seem to come off any worse when pregnant. Relief from fits obtained during pregnancy is not likely to persist. There appears to be some evidence that fits are more frequent when the foetus is a male. In a few cases the fits seem to be directly related to labour, to the puerperium or to lactation. Burnett considers that the course of epilepsy during pregnancy will depend on the interplay of various factors, differing in each individual case. Thus, he cites water retention, CO_2 deficiency and hypoglycaemia as conditions known to occur in pregnancy which may predispose to fits, and to these he adds possible altered hormonal relationships. As favourable factors he suggests the ketosis that occurs in the early months, and alterations in the posterior pituitary. Such E.E.G. observations as have been made indicate that cortical dysrhythmia is likely to be relatively more prevalent in pregnant women. Burnett discusses the relation between epilepsy and eclampsia, agreeing with the general conclusions of Rosenbaum and Maltby (1943). Nineteen cases of epilepsy, occurring in 16 mothers, are presented in detail, and include one of status epilepticus successfully treated by termination of the pregnancy. The occurrence of status is held to be sufficient justification for sterilization, but there is no eugenic indication for this measure or for the termination of an established pregnancy.

EPILEPSY IN CHILDHOOD.

Bridge *et al.* (1947) summarize the results of a 15-year study of epileptic children at the Johns Hopkins Hospital. They classify aetiological factors into 5 groups: hereditary, brain damage, physiological disturbances, personality maladjustments and environmental stress. Follow-up observations, over periods varying from 2 to 15 years, show that 40 per cent. have been clear of fits for a year or more, and 17 per cent. for 5 years. Hereditary, personality and environmental factors seem to have little influence on the outlook for fit control, but the reverse is true of brain injury. Residual social handicap appears to be most often due to mental retardation, rather less often to personality disturbances, and less often again to the fits themselves. This is a most important observation from the point of view of the place of the epileptic in society. Elsewhere, Bridge (1947) shows that the personality difficulties often develop during the school career. They rarely precede, or are associated with, the onset of fits, and their appearance and development could no doubt often be avoided by proper environmental conditions, the provision of which calls for expert advice and team-work. This indicates a pressing need for the comprehensive treatment of the epileptic child, for it is lamentable indeed for him to go out into the world inevitably handicapped by his seizures, and still

more heavily handicapped by temperamental difficulties which might have been prevented.

A very useful symposium on epileptic children (*The Nervous Child*, Jan., 1947) has recently appeared, and deserves careful study by all who have to deal with them. Here will be found accounts of the neuropathology and psychopathology of the group, of drug therapy, and of the provision for, and care of, epileptic children in non-residential and residential schools in America.

EPILEPSY AND CAR DRIVING.

To the question whether an epileptic should be allowed to drive a car, there would appear to be a very simple answer. In his own interests, and still more in the interests of the public, driving should be absolutely prohibited. Closer examination shows that the position is not quite so simple. Selling (1943) discusses the question from a Psychopathic Clinic attached to a Recorder's Court in Detroit. About 1 per cent. of 2,000 drivers dealt with by the Traffic Division of the court had been found to suffer from some type of convulsive seizure. Selling inclines to think that 5 or 6 years' freedom from fits should allow reinstatement of a driver, that those whose fits only occur at night should not be debarred from driving, and that all cases where the history or diagnosis are in doubt should receive neurological and psychiatric investigation. Glaser and Irons (1946) sent a questionnaire to 127 medical members of the American Branch of the International League against Epilepsy. It is clear from the replies, which were nearly complete, that informed medical opinion in the States would debar all those suffering from any type of epileptic fit from driving, that less than 1 in 10 would alter his decision even if it was clear that the patient had an adequate aura, and only 1 doctor in 7 would allow a licence to a man with only nocturnal fits, or whose fit incidence was less than one a year. Where doubt exists, 70 per cent. of the doctors would advise an E.E.G., but would agree to the refusal of a licence on an abnormal E.E.G. record without evidence of clinical attacks. In answer to the question as to the length of the period of freedom from fits before a licence should be renewed, the replies varied from 6 months (1 per cent.) to never (9 per cent.), with an average of 3 years. Glaser and Irons accept this 3-year period of freedom as a reasonable one, with the proviso of careful investigation of each case individually. They agree that night-fitters and those with auras should be debarred, and go further in suggesting that epilepsy and other conditions causing unconsciousness should be made notifiable. In practice, the diagnosis should be made on clinical grounds; the E.E.G. should only be used to supplement clinical diagnosis.

More recently, Symonds (1948) has reviewed the position in this country. He has sought official ruling on the question of people who have only had one or two fits, or who have been free for a long period, but has received no satisfactory reply. Apparently anyone who has ever had a fit is officially, permanently debarred from getting a driving licence. "Once an epileptic, always an epileptic," is a cry that has got well worked into the official, as well as the public mind. There is no legal provision for escape, and "subsequent liability is entirely a medical question." Thus, the whole responsibility is

placed squarely on the shoulders of the medical practitioner. This is playing for the safety of the public, no doubt, but it is not fair to many who may have had epileptic manifestations of some kind at some time in the past. Symonds holds that it is time that we had impartial tribunals with power to grant licences to epileptics who have been free from attacks for a specified period.

TREATMENT.

An excellent general account of the modern treatment of epilepsy is provided by Lennox and Walker (1947). Although primarily intended as a guide to the treatment of ex-service cases, it is applicable to epileptics generally. It sets out the value, from a therapeutic standpoint of various forms of investigation, lists the drugs at our command and their applicability to different types of seizure, and outlines the role of surgical, psychological and social measures.

PHENYTOIN.

Soluble phenytoin (epanutin, dilantin) has now established itself as a valuable anticonvulsant. In this country, Tullidge and Fox (1942), Butter (1945) and Burrows (1947) have reported on its use among institutional patients. Houston Merritt (1947), who introduced the drug into clinical use, considers it to be of great value in *grand mal* and in psychomotor attacks, though other observers have found it disappointing in the latter group. It has the advantage of having little or no hypnotic action. Dosage is, however, difficult, as toxic reactions are common. It is well to start with $1\frac{1}{2}$ gr. three times a day with an adult, increasing to 6 gr. a day in a fortnight, if necessary. Further increase up to 9 gr. daily may be required. When the effective dose causes toxic symptoms, a smaller dose in combination with phenobarbitone should be tried. Merritt considers that it is almost impossible to take a fatal dose of phenytoin, an observation confirmed by Nauth-Misir (1948), who reports uneventful recovery after a self-administered dose of, probably, 375 gr.

Parke Davis and Co., who market the drug under the name of epanutin in this country, and of dilantin in America, have published a very useful and comprehensive booklet, giving an account of its employment in the treatment of *Convulsive Disorders* (1945). They describe its history, chemistry and pharmacology, its clinical value in various forms of attack and the incidence and meaning of failure in certain cases. They compare its results with those of phenobarbitone, and deal at length with its toxic reactions. The whole book is well documented and attractively produced.

MESANTOIN.

Several American investigators have carried out clinical trials of a closely allied drug, methyl-phenyl-ethyl-hydantoin, mesantoin. Kozol's last report (1947) concerns 140 patients. He finds mesantoin useless in *petit mal*, but two-thirds of the patients averaged a 95 per cent. improvement in the incidence of major fits, 26 having been free for over a year. In 6 cases a morbilliform rash appeared during the first month of treatment, but Kozol finds that this can be avoided by starting with very small doses. The average dose was

0.6 gm., but larger doses were often given, and were only limited by the development of drowsiness. Owing to the rarity of toxic symptoms, the drug can be given in larger doses than phenytoin, with correspondingly improved anti-convulsant effect. The fact that 38 of the patients had been receiving phenytoin at the same time detracts somewhat from the value of the article. A similar criticism applies to Loscalzo's 3-year study (1947) of 67 patients taking mesantoin in combination with phenobarbitone. With an average dose of 0.4 gm., toxic symptoms were minimal. *Petit mal* and psychomotor attacks were not affected, though Harris and Otto (1947) found that 13 out of 24 patients with the latter form of attack were completely freed by mesantoin. Lennox (1946b) concludes, after experience with 35 patients, that in a third of *grand mal* cases mesantoin is superior to phenytoin, either in reducing the frequency of fits, or in obviating unpleasant toxic symptoms due to the latter drug.

(An editorial note at the end of Kozol's paper states that a death from aplastic anaemia has since been reported.)

TRIDIONE.

Tridione, trimethyloxazolidine dione, is a new and effective drug, synthesized in 1944, that has yet to settle down into its place in the treatment of epilepsy. Perlstein (1947) treated 147 cases with varied neurological manifestations over a period of 2 years. He found the drug most effective in *petit mal*, especially of the idiopathic type, clinical improvement being matched by corresponding betterment in the E.E.G. In major epilepsy the results were conflicting. Toxic effects, mostly in the form of visual disturbances, were rare, especially in children. In the treatment of 100 sufferers from *petit mal*, Kloeck and Ledeboer (1948) compare the results of tridione with those obtained by the use of the ketogenic diet. Tridione is, they find, of little value in patients over 20, but even in children it is not always successful, and cannot replace the ketogenic diet, and they recommend a combination of the two forms of treatment.

In two comprehensive papers Lennox (1947d) and Davis and Lennox (1947) have given an excellent account of the clinical value of the drug, and of its untoward effects. A group of 245 epileptics with a wide range were studied over a period of 2½ years. The seizure classification was into *grand mal*, psychomotor attacks and the *petit mal* triad. The latter includes akinetic or loss of posture attacks, myoclonic jerks and the common transient loss of consciousness, sometimes accompanied by a little 3-per-second muscle jerking (pyknolepsy). Among 182 patients having one or more of the *petit mal* triad, a third became seizure free, and a further 50 per cent. showed a significant improvement. The younger children did the best, a fact that becomes still more obvious if those with focal brain damage are excluded. Those with numerous attacks did as well as those with few, and omission of the drug after a time was not always followed by recurrence. Disappearance of *petit mal* was accompanied by drastic reduction or disappearance of spike and wave formations on the E.E.G. Results were equally good for pyknolepsy, akinetic seizures or myoclonic jerks. For psychomotor attacks tridione was ineffective,

but may possibly have been of value in combination with phenytoin, while for major fits it must, on balance, be regarded as mildly prejudicial. For patients with more than one type of attack, therefore, tridione must be combined with other forms of medication. Tridione is dispensed in 0.3 gm. capsules, and the daily dose may be increased, at monthly intervals, up to 4 capsules or even more. Toxic effects are dealt with at length. Photophobia occurred in about one patient out of every three, some having to wear dark glasses. It usually started a few days after medication was begun, and ophthalmological examination was consistently negative. Tolerance sometimes developed, but, in any case, the symptom disappeared rapidly with discontinuance of the drug; but only in 4 cases was the condition severe enough to call for discontinuance. One patient in 7 developed a rash. Mostly this took the form of acneiform papules on the forehead or face, but occasionally a generalized morbilliform rash called for immediate omission of the drug. Less common complaints were nausea, difficult behaviour and fatigue.

The effect on the blood calls for more detailed report. Harrison *et al.* (1946) record the case of a girl of 16 who was admitted to hospital after 6 months' tridione treatment. Her white blood count was 1,000, and red cells numbered 3,100,000. Tridione was stopped and vigorous measures adopted to combat the anaemia, but the patient died in 5 weeks. Mackay and Gottstein (1946) had a similar experience with a woman of 26. Ten months after she had started taking tridione she complained of headache and fatigue. Five days later she was admitted to hospital with an R.B.C. count of 1,550,000, and a white count of 4,250, of which neutrophils were only 15 per cent. Tridione was stopped, but she died 12 days later of aplastic anaemia and agranulocytosis. In the same issue of the *American Medical Journal* in which these two fatalities are reported, there is an illuminating letter from Greaves (1946). He tells the story of a neutropenia following the administration of tridione, of rapid recovery when the drug was stopped, of a further fall to 900 W.B.C.'s (neutrophils 13 per cent.) when tridione medication was reinstated, and again a quick return to normal after its omission. In this country Braithwaite (1948) records a fatality in a boy of 11. After 7 weeks' treatment with tridione he became ill with gingivitis and pyrexia, and considerable gland enlargement. Twelve days later the red count was 2,730,000, and the white count 800; no neutrophils could be found. He died of agranulocytosis 9 days after that. Another death, in a girl of 9, after only 4 weeks' treatment with tridione, does not appear to have been reported in the medical papers. Apparently the cause of death was exfoliative dermatitis.

Davis and Lennox (1947) examined the blood of 127 patients taking tridione at regular monthly intervals, and review the results of over 300 examinations. The only significant changes are a tendency to neutropenia and eosinophilia, and a slight increase of lymphocytes. Neutropenia is found in 6.3 per cent. of all patients, and repeated examinations show that it develops gradually, and that regular monthly testing would ensure detection early enough to avoid disaster. They conclude that tridione should not be prescribed if there is a history of blood dyscrasia or drug idiosyncrasy, that monthly blood examinations should include haemoglobin estimations, leucocyte and differential white counts,

with particular attention to the presence of platelets in the blood smear, that a leucocyte count below 2,500 calls for frequent checking, and a count below 1,600 for immediate discontinuance of the drug.

An entirely different and rather disturbing report is that of Barnett *et al.* (1948). A girl of 14 had frequent attacks of *petit mal* which were entirely controlled by tridione. After 8 months' treatment generalized oedema appeared with albuminuria, low serum albumin and total protein, and hypercholesterolaemia. Blood counts were normal. Tridione was stopped, and in 5 weeks the symptoms and pathological findings had all disappeared. As tridione was the only drug that could control the *petit mal*, it was started again. In 2 months the kidney signs and symptoms recurred as before, but there was some haematuria and a moderately raised blood pressure as well. Again, the whole picture proved completely reversible within a month. A third trial of the drug was followed by an exactly similar sequence of events. The authors conclude that it is difficult not to associate tridione in this case with the production of a nephrotic type of nephritis, without, fortunately, permanent impairment of kidney function.

More recently, Davidoff (1948) has reported on the administration of tridione to 75 institutional epileptics. In *petit mal* attacks and in epileptic manifestations associated with cerebral paralysis, he finds it most successful; in the control of psychomotor manifestations it is of less value; while it is quite useless in the treatment of major fits and of myoclonus. Except, perhaps, in *petit mal* cases, improvement in E.E.G. records does not consistently correlate with clinical improvement. Generally speaking, slow waves of high amplitude are eliminated, while fast waves are unaffected. Toxic reactions are recorded in some detail. Mild fatigue, headaches, irritability or indigestion occurred in 55 out of the 75 patients, blurring of vision or the "glare phenomenon" in 49, marked fit increase in 9, stupor, confusion or excitement in 7, dermatitis in 11, and fall of systolic blood pressure to less than 85 mm. in 7. Forty-six cases showed decrease in the polymorphonuclear count; in 40 of these the condition was not severe and the count rapidly returned to normal when the drug was discontinued or reduced. In 6 cases the blood changes were more severe and prolonged, but there were no fatalities. There was a general inverse relation between toxic reactions and clinical improvement. Thus the myoclonus and *grand mal* cases suffered most, the *petit mal* and cerebral spastics came off best. Davidoff considers that the toxic effects could be minimized by careful observation and dose adjustment, and that tridione is more effective in controlling attacks associated with cerebral palsy and *petit mal*, and possibly psychomotor seizures, than any other medication.

A very recent note by Briggs and Emery (1949), on their experience in the treatment of 10 cases of *petit mal* in children, makes rather gloomy reading. In 3 cases the drug was stopped because it was useless, and in 2 because of severe neutropenia. In the latter there was a further fall of neutrophils for some time after the drug had been omitted, but ultimate recovery. Biopsy in one case showed that all the elements in the bone marrow, including the red cell precursors, were affected. Another child, after 4 months' treatment, developed a nephrotic condition similar in all respects to that in the case described by

Barnett *et al.* (1948), and therefore almost certainly attributable to tridione. In this case, however, there was a fatal result.

Further reports on the clinical value and toxicity of tridione are urgently needed. Without being cynical, it is well to remember that the earliest appraisals of anticonvulsant drugs have, in the past, always been the most optimistic. Moreover, there is always a risk, albeit a very small one, of grave disaster, and unless a monthly blood count and meticulous clinical observation can be ensured, that risk should not be taken.

dl-GLUTAMIC ACID.

Price *et al.* (1943), recognizing the value of the ketogenic diet in the control of *petit mal*, decided on theoretical grounds that *dl*-glutamic acid should also prove effective. Accordingly, they gave from 12 to 20 gm. daily, in capsules, to 8 patients, and noted that seizures associated with slow-wave activity (*petit mal* and psychomotor attacks) were decreased in frequency, while all the patients became more alert mentally and physically. Major fits were unaffected, and there were no toxic effects. In a subsequent communication Waelsch and Price (1944) conclude that the therapeutic effects can be ascribed to the L(+) glutamic acid. Further clinical reports are obviously needed, but the greater efficiency of tridione in *petit mal* has probably ousted glutamic acid from the therapeutic shelf.

DELVINAL SODIUM VINOBARBITAL.

There is little general agreement about the drug treatment of status epilepticus. Few physicians see a sufficient number of cases to give a balanced opinion, and the establishment of adequate controls is almost out of the question. Morphine and hyoscine were commonly used a generation ago; chloral, paraldehyde, somnifaine, sodium amytal, soluble phenobarbitone and chloroform inhalations are probably the most favoured remedies now. The medical officers of really large institutions for epileptics are in the best position to give clinical impressions of value, and Davidoff *et al.* (1948), working at the Craig Colony, have recently reported striking success with delvinal sodium vinobarbital given intramuscularly or, better still, intravenously. Out of 25 patients suffering from status or from severe serial seizures, success was obtained in 23 with a minimum of post-seizure mental or physical sequelae. An initial dose of 10 gr. is advised, but this can be repeated or, with adults, increased without fear of toxic effects. The results obtained are, they believe, very much better than those following the use of the previously recognized remedies.

KETOGENIC DIET.

It would be interesting to know if the ketogenic diet is still being used in this country. The difficulty of obtaining the requisite extra fat has probably led to its disuse. At best it is rather a cumbersome procedure, needing continuous and meticulous supervision. How far it is being used in other countries, it is not easy to say, but it is not without its enthusiastic advocates. As we have seen, Kloek and Ledeboer, in Holland (1948), regard it as far more

efficient in the control of *petit mal* in children than tridione, and Petersman, in America (1946), speaking from a very wide experience, thinks it is easily the safest and most effective method of dealing with these attacks. In an attempt to evaluate different methods of non-surgical treatment of epilepsy in childhood, Keith (1947), of the Mayo Clinic, treated 149 children with idiopathic epilepsy by means of the ketogenic diet, phenobarbitone, phenytoin or with combinations of these agents. The best results were obtained with the ketogenic diet, with or without drugs. Phenobarbitone or phenytoin, either singly or in combination, were about half as effective. The patients were all the subjects of *grand mal* or *petit mal*, or both, but unfortunately Keith does not correlate successful treatment with the type of fit. In a follow-up study, however, of 190 patients who had been treated by the ketogenic diet between the years 1921 and 1930, he finds that over a third had been free from attacks for periods of 4 up to 22 years, and the proportion of successes was the same in *grand mal* and *petit mal* cases.

E.C.T. IN TREATMENT.

The possible therapeutic value of E.C.T. in epilepsy has been the subject of several papers. Taylor (1946) reports the treatment of 19 psychotic epileptics with intensive E.C.T., starting with 3 treatments weekly and gradually reducing the number, if no spontaneous convulsions occurred, to one a week. No sedative medicines were administered meanwhile. The treatment, which had been instituted to eliminate spontaneous fits, was completely successful in 17 cases, and relatively successful in the other 2. A marked decrease in the number of furors was noted, together with considerable improvement in the patients' general demeanour, and less evidence of deterioration. Caplan (1946) also treated 25 mental hospital patients with E.C.T. The average number of treatments was 27, and the average duration of the course 8 months. The reduction in spontaneous attacks was significant, but not dramatic. Even so, the effect was only transient, the fits returning with their previous incidence when E.C.T. was stopped. The psychological effect was more encouraging. In 14 patients who suffered from an associated psychosis without dementia, the symptoms were ameliorated in all but 3, and in 19 cases of epileptic twilight states with violence and destructiveness the condition was satisfactorily brought to an end by E.C.T. in all but one. Caplan concludes that E.C.T. is of value in epileptics with associated psychosis or liability to periodic twilight states, and further suggests that in non-institutional patients an "out-patient fit" at regular intervals would, in selected cases, greatly reduce the liability to spontaneous fits in daily life with their attendant risks and social handicaps. Relief of dangerous clouded states in epileptics was also found by Kalinowski (1947), who applied E.C.T. successfully in the break-up of psychic equivalents generally, and found it most effective in dispelling minor mental disturbances in unco-operative and quarrelsome patients. The rise in convulsive threshold after an induced fit would appear to indicate E.C.T. in patients with regular and predictable attacks.

Caplan (1946) deals with the question of fracture of dorsal vertebrae in induced convulsions. He claims that, apart altogether from E.C.T., a third

of male epileptics subject to frequent or severe major fits show evidence of such fractures. An equal proportion of fractures is found in non-epileptics who have had a course of induced convulsions, but the incidence is materially less for convulsions electrically produced than for those induced by cardiacal, which are more severe. Those patients whose spasm are in extension during the attack are the least liable to come to harm. In any case, these fractures are not liable to give rise to any inconvenience or disability.

THE SOCIAL SIDE.

Rehabilitation has now elbowed its way into a premier place in therapeutics. In epilepsy its recognition is of peculiar importance, for epilepsy is a complaint that carries with it social handicaps out of all proportion to the nature and extent of its clinical manifestations. Up till recently the state took no official cognizance of an epileptic, unless he was a child of school age, or was certifiable as mentally deficient or insane. When, however, the Disabled Persons (Employment) Act (1944) came into force, the field became very much wider. By August, 1946, about 7,000 epileptics had registered as Disabled Persons, of whom about 6,850 were at that time in employment. The Ministry of Labour officials have found the task of finding work for the remaining 1,350, and for others who have subsequently registered, a very difficult one, and they issued a pamphlet (1947) for the use of their Disablement and Resettlement Officers (D.R.O.'s) in approaching prospective employers. The pamphlet points out how unfair it is to regard, as many employers appear to do, all epileptics as outside the labour market. Frequent or severe fits during working hours would, of course, rule out open market employment. Many epileptics, however, only have fits at night, or at about the time of rising; others have adequate warning; others only have slight *petit mal*; still others have their attacks with a monthly or long-distance rhythm, with consistent periods of freedom. All these should be able to do useful work, and each case merits careful, individual consideration. Certain categories of work must, of course, be ruled out, notably work with live machinery, or moving vehicles, or at a height, but in a factory or shop of any size some work can be found where the accident risk is negligible. Experience has shown that many epileptics, aware of their disability and anxious to do their best, make first-class employees. Employment in pairs or groups, so that the patients could look after each other in case of fits, is suggested. With reasonable care in the selection of suitable work, the pamphlet states, the risk of accident should not exceed that of the general working population, and, anyway, under the National Insurance (Industrial Injuries) Act of 1946, employers are relieved of financial liability. Simple instructions are given, what to do, and what not to do, in the event of a fit, including advice that water, brandy and medical aid are unnecessary. There is a recommendation that his fellow workers should be advised beforehand of the possibility of an epileptic having an attack. When one occurs, one member of the staff, and only one, should attend to him, thus avoiding the general loss of working time which disturbs employers so much. Finally, every epileptic should be encouraged to keep in touch with a doctor, and to take any medicines prescribed with unfailing regularity.

The dissemination of this pamphlet, especially where it has been reinforced by personal approach to the employer, has helped to find work for a good many epileptics, though all too many employers are consistently unco-operative. For those epileptics who are not fit for open market employment, the Ministry, in conjunction with the Disabled Persons' Employment Corporation (D.P.E.C.), is providing sheltered employment in Re-employ Factories. It is understood that about 30 of these factories are now working, and that the labour force includes 96 epileptics. At some factories there is a reluctance to find a place for epileptics among the other disabled workmen. In a few areas a start has been made by the D.P.E.C. in arranging for work in their own homes, for epileptics and other disabled persons whose disability is too severe to allow their going out.

Two American articles provide more detailed information about the employment and employability of epileptics. Lennox and Cobb (1942) reported on 1,000 epileptics of working age (which means, presumably, 16 to 60) who were receiving medical treatment either privately or at clinics. These were not found to show any unusual incidence of general organic disease, although poor posture and poor physique were rather more common than they should have been. Muscle paralysis was found in 0.6 per cent., involuntary muscle movements in 4.6 per cent., impaired co-ordination in 7.2 per cent. and muscular weakness in 8.2 per cent. (There is overlap in these and in Lennox's subsequent figures.) All these disabilities were, of course, commoner in symptomatic than in idiopathic epilepsies. Lennox concluded that some 9 patients out of every 10 had average muscular strength and control. On the mental side, 10 per cent. showed gross deterioration, and 70 per cent. were judged to be mentally normal. The epileptic temperament was not present in more than 10-15 per cent., and most of these showed some degree of mental defect as well. Summing up, and taking into account cases with severe or very frequent fits, Lennox concluded that at least three-quarters of the series should be fit for employment. This estimate finds confirmation in the employment record. Over 93 per cent. of the whole had been employed at one time or another, and 75 per cent., if housewives and students are included, were actually at work at the date of enquiry. Of those gainfully employed, no less than 1 in 7 were in the professions, as doctors, clergymen, artists, lawyers, and teachers. Other forms of employment showed a general scatter, and unskilled work was not nearly as common as one would expect.

Hibbard (1945) had the task of screening 250 ambulatory epileptics for job replacement. Of these, 80 per cent. were found to be employable under normal conditions, 10 per cent. needed sheltered employment or a course of rehabilitation and readjustment, while the remaining 10 per cent. were regarded as unemployable. Of the 200 for whom work had been found, about a third were in unskilled jobs, a third were skilled workmen, and a third white-collar workers. That no professional worker appeared in this survey is, of course, due to the different basis upon which the group was built. In Lennox's survey the common basis was the receipt of medical treatment; in this case it was presumably the search for work.

In this country articles on the place of epileptics in industry have been published by Mona Thomas (1948), Halstead (1948) and Fox (1948a).

If the social handicaps consequent on epilepsy are to be understood and effectively combated, it is essential to start with the child. We have already noted that Bridge (1947) found that temperamental difficulties are increasingly evident in the later years of the school career, and much subsequent trouble could be avoided if, by an understanding of their origin, they could be prevented. Comparatively few children, Fox (1948b) believes, possess what has been described as the epileptic temperament. In certain cases there may be periods of irritability or moodiness preceding or following fits, or occurring independently of fits. These are part and parcel of the epilepsy, and are not usually amenable to psychological or social treatment, though they may in some cases be controlled by anticonvulsant medication. More often the maladjustment is due to the unfortunate attitude of society, and for this parents, teachers and school-mates must often be held responsible, and the early correction of this attitude is of crucial importance. In school certain limitations may be necessary to eliminate risks consequent on fits, but these should be reduced to a minimum. Overprotection must be avoided, and the aim should be to treat the epileptic child in exactly the same way as his fellows. Fits should be regarded, both by teacher and classmates, as not essentially different from any other physical handicap. When they occur, they should be taken as a matter of course, without emotion and with the least possible disturbance. If the teacher can retain an outward calm, the other children will not be upset or alarmed. Of still greater importance is the position in the home. The parents must be told that epilepsy is a physical disorder, usually unaccompanied by mental abnormality, and with a far from hopeless prognosis if early expert advice is sought and consistently followed. Overprotection is again the common mistake, and the child must be encouraged to indulge, as far as possible, in the same activities as others. Most parents are apprehensive about fits, many are ashamed of their child's disability, and to some it brings a feeling of guilt sooner or later, unless the parents can conquer or conceal their feelings, this apprehension, shame and guilt will be communicated to the child with disastrous results. Annoyance at having an epileptic child sometimes leads parents to treat him harshly, but overindulgence is a much more common failing, and one which makes him unpopular with his brothers and sisters. It is easy to see that he may become aggressive, sullen or moody, may develop a strong sense of inferiority or a feeling of loneliness, or a tendency to anti-social conduct. Maladjustment may lead to more fits, and so a vicious circle is set up. Early rectification of the parents' attitude will make all the difference to the child's future. Fox also discusses the question of exclusion from school, a question that can only be answered by full individual consideration. Frequent or severe fits in school, especially if accompanied by injury or incontinence, marked inability to get on with others, defects of intelligence, grossly adverse home conditions will point towards exclusion, but the great majority of epileptic children should be retained in ordinary schools. If the teacher has the right personality and the right approach, no harm will come to the other children. A residential special school will provide more effective

medical supervision, and also an environment in which the sense of inferiority will disappear, as the epileptic realizes that he and his fellows are all in the same boat.

From the vantage point of the Ministry of Education, Henderson (1948) writes on the incidence of epilepsy in children of school age. From a survey of about one-third of all the schoolchildren in the country he is unable to produce sufficient figures of the overall incidence to be convincing, as records of all cases are kept by few School Medical Officers. The number of children requiring residential school treatment on account of their epilepsy is more surely determined at about 0.3 per 1,000. The present accommodation for about 600 children meets less than half the need, and over 300 children, educable but excluded from school, are at present in their homes receiving no education. Many of these are mentally retarded or physically handicapped as well as being epileptic. Henderson quotes the results of intelligence tests carried out on groups of epileptic children in two areas. In both groups the majority of the children have I.Q.'s below 70, a result that once again illustrates the need for defining as exactly as possible the selective factors at work in the constitution of the group to be surveyed. Henderson epitomizes the policy to be adopted if epileptic children, and adults, are to adequately treated, under 5 heads :

1. Ascertainment of all epileptic children during school years.
2. Adequate educational provision for all types. The large majority should, of course, remain at ordinary schools.
3. Medical treatment by modern methods.
4. Effective after-care, especially with regard to employment.
5. A more enlightened public and professional opinion.

This is an excellent programme. As children leave school, medical treatment should be integrated with the after-care service, so that every ascertained epileptic should have the advantage, not only of expert medical investigation and treatment, but also of social investigation and treatment from the same centre. Regional epilepsy clinics are thus envisaged, staffed by a neurologist and a trained social worker, working together on each individual case, and enlisting the aid, where necessary, of the D.R.O. Such a clinic was started four years ago by the L.C.C. at St. John's Hospital, Battersea. McFie (1948), in a report on its work, states that the majority of cases with which it has had to deal have suffered from epilepsy for a considerable time, and have encountered difficulties in the social sphere. Some of them had been in mental hospitals. Out of the first 100 patients, 8 were definitely mentally defective ; 12 subnormal in intelligence, but able to hold down simple jobs ; 10 had to be admitted (or readmitted) to mental hospitals ; 16 others had serious psychiatric conditions. Nevertheless, more than half were normal in personality and intelligence, a higher proportion than might have been expected. Twice as many men attended as women, and the largest age group was between 20 and 30. The patient is first interviewed by the social worker, and at the end of the medical interview, social worker and doctor review the case together. McFie believes that it is most important that the patient should be conscious of this close and continuous co-operation. A home visit

is an essential part of the scheme. This often discloses vital information about the epileptic, and gives an opportunity of counsel to relatives who sometimes suffer as much as he does from the consequences of his complaint. Cases needing prolonged psychological treatment are referred to a mental health clinic, and, when a patient has become well stabilized, he may be transferred back to his own doctor. A large proportion of the patients were out of work when they came to the clinic, but most of those regarded as employable have since found work. The D.R.O.'s have been anxious to help, but usually take a pessimistic view of the possibilities, and, as a matter of fact, patients have often found employment on their own account. Looking back, McFie considers that the most important contribution of the clinic has been to give the patient renewed courage to face his problems and to search for work. Personality problems are the greatest difficulty, and McFie agrees that many of them are due to mishandling in childhood. She is clear, moreover, that the greatest barrier to success is the general attitude of the public to epileptics.

A more enlightened public and professional opinion is the last requisite in Henderson's 5-point policy, and no one who has had much experience of the social problems of epileptics can doubt its importance. Epileptics are the subjects of widespread ignorance, and of erroneous generalizations, almost always of a gloomy nature. Common beliefs are that they are dull, deficient and liable to deteriorate, awkward in temperament, of criminal tendencies, unemployable and incurable, and should be segregated. The prevalence of such beliefs obviously means a serious and unnecessary addition to the inevitable social handicap that must accrue from a liability to fits. In the United States there are two large societies, the American Epilepsy League and the National Association to Control Epilepsy, whose principal objects are to dispel the prejudice and error about the complaint. Both societies have a considerable literary output. There are pamphlets addressed to the public generally, or especially designed for different sections of the public, articles in the medical and lay press, and the two popular books on epilepsy, by Lennox (1946) and Putnam (1945), already referred to. In addition, lectures, wireless talks and films have been widely used to make known the simple facts about epilepsy. One cannot doubt that these are effective weapons in the fight to give the epileptic his fair place in the community.

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MENTAL DEFICIENCY.

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HEREDITY AND MENTAL DEFICIENCY.

DISCUSSING the relationships between heredity and mental deficiency, Allan *et al.* (1944) note three categories: (1) conditions, not defined at present, in which only genes affecting mentality are involved; (2) genetic conditions affecting mentality primarily, and involving other functions; (3) genetic conditions primarily affecting other functions, but also involving mental functions. Under the second heading they include amaurotic and juvenile family idiocy, Niemann-Pick's disease, Schüller-Christian syndrome, Gaucher's disease, gargoylism (Straus *et al.*, 1947; a sex-linked type is described by Nja, 1946), phenylpyruvic amentia and mongolism (Halperin and Curtis, 1942), all of which in the authors' views are recessively inherited. Under the third category they include epiloia, keratosis follicularis (Darier's disease), von Recklinghausen's neurofibromatosis, Morquio's disease (Farrell *et al.*, 1942), anhydrotic ectodermal dysplasia (Halperin and Curtis, 1942a), albinism, Waggoner and Scharenburg's (1943) idiocy with agenesis of white matter, Jervis' (1942) familial type of mental deficiency akin to gargoylism transmitted by rare recessive genes, cases of sex-linked idiocy due to recessive or dominant sex-linked transmission, which they describe in some detail, Roberts' (1937) sex-linked microphthalmia and certain types of microcephaly (Hanhart, 1943; Halperin, 1944).

Benda (1943) has given the name oligoencephaly to a type of familial mental deficiency which is associated with a number of stigmata of degeneration and pathological evidences of "spinal dysraphism." He collected 9 pedigrees of the condition in 2 to 5 generations, with 40 cases (inheritance dominant). He regards it as a hereditary developmental disorder. Marchand (1947) is of the opinion that hereditary forms of epilepsy will often be associated in other members of the family with signs of *status dysraphicus*, such as spina bifida. Excessive skin pigmentation, congenital ichthyosis, fibrolipomatous tumours, iris coloboma and cleft palate are neuroectodermal malformations that may also be found. Touraine (1947) has proposed the term "oligophrenic ectodermosis" for a group of hereditary skin anomalies associated with mental defect.

Keith (1943) has described a type of familial cerebral degeneration with cortical atrophy, akin to Krabbe's diffuse infantile familial cerebral sclerosis. Accounts of various features associated with tuberosc sclerosis are to be found in the literature (Lichstein and Solis-Cohen, 1943; Ross and Dickerson, 1943; Wolinetz and Daum, 1946; Fattovich, 1947; Thiébaud *et al.*, 1947; Marchand *et al.*, 1947; Lahdensuu, 1947).

Martoe and Bell (1943) have reported a pedigree in which 11 male imbeciles in two generations were born to mothers of normal intelligence. In spite of certain difficulties, they believe that the mental defect was due to a sex-linked recessive gene.

Friedman and Roy (1944) cite an unusual family syndrome in which a family of six "feeble-minded" children were born to normal parents who were cousins. The ages of these children ranged from 7-17, and the mental ages were less than 3. Strabismus, extensor plantar responses, speech defect and club-foot formed part of the syndrome. Arachnodactylia, sometimes associated with mental deficiency, is considered to result from the union of pathological genes originating through mutation (Greiner and Varga, 1945; see also Schneider, 1945; Parker and Hare, 1945, and Schachter, 1947).

Fairweather and O'Sullivan (1947) reported the occurrence of gastric dilatation, megacolon and coeliac syndrome in idiot twins.

Pearse (1946) gives the proportion of first-cousin parents among 1,280 institutional defectives as 1.9 per cent. as compared with 0.61 per cent. in a group of all types of hospital patients. There is no doubt that in different localities considerably different estimates will be made, as, for example, in Sjögren's investigations (1948) in a West Swedish population, where the frequency of consanguinity between the parents of oligophrenics was found to be 15.5 per cent., up to and including second cousins 11.3 per cent., and between first cousins only, 5.6 per cent. (± 2.7 per cent.).

In a report on the medical and psychological findings in the parents and sibs of 338 institutional defectives, Halperin (1946) confirms the work of other writers (Lewis, 1929 and 1948; Roberts *et al.*, 1938) that high-grade defectiveness has a more familial distribution than low-grade defectiveness. Thus 63 per cent. of the parents and sibs of idiots and imbeciles were average and above average as against 30 per cent. of the parents and sibs of morons and borderline cases. In a Merseyside survey, Jones (1947) found that nearly 60 per cent. of the children of two subnormal parents were also subnormal, that over 40 per cent. of the children where only one parent was subnormal were subnormal, and where both parents appeared to be normal, 30 per cent. of the children were subnormal.

Roberts (1947) estimates that, on the average, parents of I.Q. 130 will have only 0.1 per cent. of children with an I.Q. below 70, plus the chance that 4 in 1,000 will be idiots or imbeciles. Similarly, with parental I.Q. of 115 the chance of having a child with an I.Q. below 70 is 0.6 per cent.; with parental I.Q. of 100 the chance (of children with I.Q. below 70) is 2.3 per cent.; with parental I.Q. 85—a chance of 6.7 per cent.; with parental I.Q. of 70, 15.9 per cent.; and with parental I.Q. of 55 there is a 30.9 per cent. chance of the children's I.Q. being below 70.

The problem of intelligence and fertility has recent topical interest (*cf.* Burt, 1946, 1947; Roberts, 1947*a*). Thus Halperin (1946) gives the mean numbers of sibs per patient according to various parental crossings as: defective $\times$ defective, 5.6; defective $\times$ inferior, 5.5; inferior $\times$ inferior, 4.9; inferior $\times$ average, 4.4; average $\times$ average, 3.4; average $\times$ above average, 2.8; above average $\times$ above average, 2.3.

Possible "restitution factors" have been mentioned by Penrose (1947) and Thomson (1947), for though 60 per cent. to 70 per cent. of the variants might be due to inheritance it was still possible that the remaining 30 per cent. to 40 per cent. were due to educational, environmental or nutritional factors. Similarly, Schachter (1947) noting a strong correlation between the mental level of the child and the economic situation of the parents, concludes that the raising of social standards would contribute extensively to a raising of the individual mental level. Pedersen (1946) found that one third of a group of unmarried mothers came from the dullard class and suggested that sterilization of dullards after illegitimate pregnancy might be considered. Another order of "restitution factor" is indicated by Savage (1946), who showed that the infant mortality rate was inversely related to maternal intelligence.

Phenylketonuria is the subject of fairly extensive reviews by Følling *et al.* (1945), Munro (1947) and Penrose (1946), of whom the first writer assumes that the condition is due to a single recessive gene which has four distinct actions, namely, on the central nervous system, accounting for the low-grade oligophrenia, muscular hypertonia and other neurological signs; the skin, with its pallor and blonde hair; the lack of pigmentation of the eye; and general metabolism, with the presence in the urine of phenyl-pyruvic acid. The primary step in the disorder is a transformation of the natural *l*-phenylalanine to *d*-phenylalanine which subsequently gives rise to phenyl-pyruvic acid. Some human and animal experiments supporting this view are quoted. One case accompanied by serious functional disturbances of the liver with a decrease of 27 per cent. in the B.M.R. was quoted by Delay and Pichot (1947).

An alternation of rapid and slow waves has been noted in the EEG by F. and E. Gibbs (quoted by Delay *et al.* (1947)).

The pathological chemistry of phenyl-ketonuria is discussed by Penrose, Følling *et al.*, and Delay *et al.* (1947a).

Penrose has investigated the relationship between phenyl-ketonuria and the blood agglutinogens A, B, O and A₁, and found indications of the presence of genetic linkage.

New cases are reported by Medlicott (1944), Lassen (1947), and Frazier (1947).

RHESUS FACTOR AND KERNICTERUS (NUCLEAR JAUNDICE).

An interesting chapter in the nosology of mental deficiency has been opened up by the discovery of antigenic incompatibility between mother and foetus in the production of erythroblastosis foetalis. Here is a disease which is genetically determined only in the sense that trouble arises primarily through incompatibility between what has come through from the father's side (Rh +) reacting with the maternal blood (Rh -) through the placental barrier. It is a striking example of disease caused by heredity interacting with maternal environment. Various workers (Yannet and Lieberman, 1944, 1946; Snyder, Schonfeld and Offerman, 1945) have suggested that this incompatibility is a *direct* cause of mental deficiency. Others (Penrose, quoted by Race, 1946; Cappell, 1947, 1948; Scholl *et al.*, 1947) admitting that survivors of erythroblastosis foetalis are occasionally defective are inclined to believe that Rh

incompatibility is not a frequent cause of mental defect. Schmorl (1903) first applied the term "Kernicterus," i.e. nuclear jaundice, to that small proportion of infants dying from erythroblastosis foetalis who showed evidence at post-mortem of cerebral damage, especially in the basal ganglia. Of 120 cases of jaundice of the newborn, 6 instances of this condition were found. Stiller (1947) followed up 35 patients known to have had erythroblastosis, 6 of whom had died. There was no apparent correlation between the degree of clinical involvement of the central nervous system and the pathological picture. Of the 29 living children 4 (15 per cent.) showed signs of involvement of the central nervous system that might be attributed to kernicterus; 2 of these 4 showed evidence of involvement of the central nervous system in the neonatal period. The author concludes that transfusion therapy is not likely to help a brain that has already been damaged.

Contesting this view, Cappell (1948) compares the effects of transfusion therapy soon after birth in 30 infants without any neurological sequelae, and a larger series of cases of icterus gravis treated mainly at a later stage, of whom about 22 per cent. showed some residual nervous sequelae, such as general backwardness. Similar figures are given by Parsons (1947). Montgomery (quoted by Cappell, 1948) gives the incidence of nuclear damage in post-mortems of fatal cases of icterus gravis as about 30 per cent. Cappell considers that anoxaemia in the immediate post-natal period may be a determining factor.

Wiener and Brody (1946) point out that although 10 per cent. of marriages occur in which Rh — mothers mate with Rh + fathers to produce Rh + children, the incidence of erythroblastosis is approximately 1 in 300, presumably because sensitization is not invariable. Erythroblastosis can occur when the mother is Rh +, and in the authors' view this is due to iso-immunization to the ordinary A-B blood group factors. Sensitivity in the mother must therefore be proved by demonstrating anti-Rh factors before presuming that the Rh factor is operative. The authors believe that kernicterus is due to bivalent antibodies (agglutinins) in the mother's serum crossing the placental barrier through a "milking" effect of the uterus during parturition. These antibodies have large molecules and are therefore not likely to traverse the placenta during pregnancy, so the pathological effects (jaundice and toxicity) are not usually apparent until a little time after birth. Their action is to cause agglutination thrombi in vessels where the circulation is slow, which in the liver produces jaundice and in the brain kernicterus. This view is contested by Parsons and Baar (1948), and Cappell (1948a).

Pentschew (1948) suggests that among the liver functions damaged is the production of a substance ("antihypoxydin") indispensable for the oxygen-metabolism of the brain, especially of areas peculiarly susceptible to oxygen lack, e.g. pallidum, cornu Ammonis, striatum, dentatum, corpus subthalamicum, olivary body and nuclei in the floor of the fourth ventricle. He proposes the term "encephalopathia posterica infantum" to embrace the syndrome involving disturbances of these structures, and considers that the clinical features in many cases are identical with those of Vogt's disease or status dysmyelinisatus, and Coquet (1944) is of a similar opinion.

Coquet (1944) has described the subsequent clinical course of 5 cases—4 showed extra-pyramidal signs and in all these was a familial history of icterus gravis. The early onset of rigidity (permanent or intermittent) with marked tendency to opisthotonos or torsion spasms is noteworthy. Involuntary movements of the face and mouth, e.g. suction, mastication, sudden tongue-protrusion, grimacing, dropping of the jaw, and deglutition, in contradistinction to the more normal distribution in choreo-athetosis of arm and hand movements, are characteristic. Sialorrhoea, myoclonic spasms, convulsive attacks, deaf-mutism, scissors posture of the legs, delayed progress in walking and talking, kyphosis, mesencephalic epilepsy and sudden losses of tonic control with episodes of opisthotonos were noted in individual cases.

The important question yet to be solved is the quantitative importance of Rh incompatibility as a cause of low-grade mental deficiency. Yannet and Lieberman (1944) determined the Rh blood group of 109 idiot and imbecile children, together with that of their mothers, with the following results:

I. Special groups (total 53):

Mongols, 23	} Only 4 proved to be Rh + with Rh—mothers, i.e. normal expectation in a random sample.
Spastic diplegia, 13	
Post-natal infections, 8	
Birth trauma, 4	
Cranial anomalies, 3	
Cerebellar ataxia, 1	
Amaurotic idiocy, 1	

II. Undifferentiated group (total 56):

Eleven Rh + with Rh — mothers (in contrast to the normal expectation of 5.15).

Snyder *et al.* (1945) found 11 such cases out of 68 similar undifferentiated defectives.

These figures suggest that Rh incompatibility might be about half as important numerically as mongolism, as a cause of mental deficiency among institutional defectives.

Klingman and Carlson (1937) found a history of neonatal jaundice in 6–7 per cent. of cases with delayed motor development and extrapyramidal rigidity, but Bakwin and Wiener (1947) do not believe that iso-immunization is an important cause of athetosis. Forster and McCormack (1944) have reported two cases of kernicterus without erythroblastosis, suggesting that the Rh factor may not be as specific as it is considered to be. Yannet and Lieberman (1945 and 1948) have brought forward some evidence to show that undifferentiated types of mental deficiency may be due to ABO iso-immunization. It is suggested that the pathology of ABO iso-immunization is fundamentally different from that found in Rh iso-immunization.

CONGENITAL MALFORMATIONS.

Warkany (1945) summarizes recent knowledge as to the etiology of various malformations indicating two distinct periods in foetal life:

(a) The first 10 weeks which is the period of organogenesis and during which time the severe malformations are liable to occur, and—

(b) from the third month to term, when the organs are to some extent differentiated, so that adverse factors are likely to produce disease or retarded development.

He considers that some conditions, e.g. cleft palate and syndactyly, may be produced either by genetic factors, maternal avitaminosis (riboflavine) or X-radiation. Among the environmental influences operating *in utero* he cites infections (e.g. rubella, syphilis and toxoplasmosis), X-rays, toxins (alcohol, lead, parental tuberculosis and contraceptives) and malnutrition (*cf.* Corner, 1944).

X-rays are credited with the power to produce mental defect, microcephaly and various osseous deformities, especially of the humerus, radius, ulna, fibula and ribs. In pigs a lack of vitamin A in the mother's diet has been noted to cause epiphthalmia, cleft palate and accessory ears in the offspring (Warkany and Schraffenberger, 1933 and 1937), and in rats a lack of vitamin A has resulted in various ocular defects in the offspring (Warkany and Schraffenberger, 1944). Maternal ariboflavinosis may produce various skeletal deformities in the offspring (Warkany and Schraffenberger, 1944a), which are incompletely modified when the maternal diet is supplemented with liver but deprived of vitamin D (Warkany, 1943).

Burke *et al.* (1943), in a series of nutritional studies concluded that the majority of infants with marked congenital defects, all premature and functionally immature infants were born to mothers whose diets during pregnancy were very inadequate. Gesell and Amatruda (1947) have drawn attention to a form of ocular maldevelopment, retrolental fibroplasia, that is closely linked with extreme prematurity.

Penrose (1946) considers that advancing maternal age is significantly related to the incidence of such abnormalities as anencephaly, spina bifida and congenital hydrocephaly. Primogeniture is also of some etiological importance.

Discussing embryological aspects of various forms of congenital anomalies of the neuraxis, Campbell (1948) is of the opinion that the Arnold-Chiari malformation and teratoid formations may be due to hyperthermia in the mother between the third and fifth weeks of gestation.

SURGICAL ASPECTS.

Michelsen (1943) discusses the indications for surgery in various cranial and intracranial malformations, e.g. hydrocephalus, for which endoscopic coagulation of the choroid plexus may be suitable; basilar impression or platybasia, in which suboccipital decompression and laminectomy of the upper two cervical vertebrae may be indicated; and for the Arnold-Chiari malformation with herniation of the cerebellum and medulla into the spinal canal, for which simple decompression of the posterior fossa and of the upper cervical cord is advised.

Circumscribed areas of microgyria, localized porencephalic cysts, secondary subdural haematomata, some intracranial aneurysms, various types of angioma, and meningo-encephalocele may provide indications for surgical treatment.

Ingraham and Matson (1944) write convincingly on the successful surgical treatment of subdural haematoma and of its relationship with infantile hydro-

cephalus. Ninety-eight cases between 1937-43 were observed at the Boston Childrens' Hospital. In half the cases there was a history of head injury and in 28 there was severe birth trauma (an underestimate in the writers' views). The majority were males and under 6 months old. Characteristic symptoms were (1) failure to gain weight, refusal of food, irritability, abnormal temperature swings; (2) accelerated increase in size of head; (3) a history of difficult labour. Diagnosis is helped by X-ray, abnormal neurological signs, such as convulsions, increased motor tone and hyperactive reflexes, and puncture through the lateral wings of the anterior fontanelle. The relative incidence of different signs has been estimated by Statten (1948). Flew (1944) has described a case in this country (*cf.* also Puech *et al.*, 1947 and 1947a).

Caffey (1946) has noted multiple fractures in the long bones of infants suffering from chronic subdural haematoma. Kaplan (1947) is of the opinion that "any infant who has been progressing normally up to the age of 4 or 5 months and then begins to have periods of lethargy, convulsions, vomiting, restlessness and disproportionate enlargement of the head should be suspected of a chronic subdural haematoma."

Babson (1944) has reported three cases of spontaneous subarachnoid haemorrhage in infants between the ages of 18 and 30 days. Hydrocephalus developed in two of the cases. He suggests that free drainage of the blood is indicated. The author admits that the condition might be associated with subdural haemorrhage.

Simmons and Peyton (1947) have contributed an interesting paper on premature closing of the cranial sutures which, in their view, is related to microcephaly and to craniostenosis.

They propose the following classification for craniostenosis:

- A. Complete early premature synostosis of the cranial sutures (oxycephaly).
 1. Oxycephaly without facial deformity.
 2. Cranio-facial dysostosis of Crouzon.
 3. Acrocephalosyndactylism.
 4. Delayed oxycephaly (onset after birth).
- B. Incomplete early synostosis of the cranial sutures.
 1. Scaphocephaly—premature closure of the sagittal suture.
 2. Brachycephaly—premature closure of the coronal suture, or of coronal and lambdoidal sutures.
 3. Plagiocephaly—asymmetrical premature closure of the sutures.
 4. Mixed.
- C. Late premature synostosis of the cranial sutures after the skull has reached or nearly reached adult size. No deformities and no symptoms.
(Not amenable to surgical treatment and not pathological.)

The obliteration of the sutures is readily demonstrated by X-ray. The authors discuss the various surgical manoeuvres possible and are of the opinion that if mental retardation is to be prevented, early operation should be carried out on the skull. They describe the use of tantalum foil to prevent bone growing too quickly across the craniectomy defect.

MATERNAL RUBELLA AND CONGENITAL DEFECTS.

The preliminary findings of Gregg (1941) as to the occurrence of various congenital defects following rubella in mothers who contracted this disease in pregnancy have been amply confirmed, and only a selected reference can be made to the outstanding features.

The main effects are on eyes, ears, heart and nervous system, and the lesions reported vary in incidence in different parts of the world.

Gregg (1945) considers that all cases show mental retardation, but noted a tendency to improvement with later development. Caruthers (1945) reported 250 cases of deaf-mutism and attributed the condition to a form of sacculo-cochlear degeneration, similar to that accounting for 70 per cent. of all congenital deaf-mutes. The deafness is incomplete, in that noises as from whistling, clapping, telephone bells, motor horns, aeroplanes in flight can be heard, but the spoken voice is inaudible. Speech is restricted to a few words, bone conduction being better than air conduction for high tones, but not appreciated at all for low tones. Apparent improvement was observed about the second half of the fourth year, as ability to concentrate increased. Martin (1946 and 1946a), who has reported the biggest number of cases occurring in this country, attempted to find the causes of deafness in deaf children who were born in the year 1940 and 1941 (after the period of a more severe rubella epidemic). She obtained particulars of 102 children, in 15 of whom the deafness was hereditary, and in 8 following meningitis, but 36 of the mothers contracted rubella during the first four months of pregnancy, and 6 others probably suffered from the disease.

Of the eye defects noted, cataract with central opacity and relatively normal periphery appears to be the most frequent, but many other conditions occur, e.g. microphthalmia (of one or both eyes), shallow anterior chamber, nystagmus, sluggish pupil reactions, difficulty in mydriasis, atrophy of the iris, subluxation of the lens, corneal opacities, strabismus, optic atrophy, pigmentary changes in the fundus, anterior uveitis, hydrophthalmia, naso-lacrymal stenosis, coloboma of iris, vitreous opacities and buphthalmos.

The heart lesions have been stated to be acyanotic or potentially cyanotic, and include patent ductus arteriosus and patent interventricular septum.

Swan (1944) reported 51 cases of microcephaly out of 77 affected cases, and in the New South Wales investigation (1945) 44 children were so affected out of a total of 52. Rarely is it a sole malformation. Others have mentioned hydrocephalus, cerebral agenesis, spina bifida, talipes equino-varus, arachnodactyly, bilobed kidney, bicornuate uterus, spastic diplegia, mongolism, persistent thymus, cleft palate, umbilical and inguinal hernia, hypospadias and cryptorchidism as occasional effects. A number of authors (Brown, 1947; Swan, 1944a; Swan and Tostevin, 1946; Caruthers, 1945) attribute to the condition sucking and feeding difficulties, malnutrition, retarded physical development, prematurity, asthenia, susceptibility to respiratory disease, purpura, severe anaemia, and pyloric stenosis.

Evans (1947) has made observations on the dental defects in 67 cases following rubella. When the mother was infected before the third month, 1 child in every 2 showed delay in eruption as against 1 in 20 of the "later

pregnancy" group. Enamel hypoplasia, congenital absence of deciduous teeth, premature eruption of permanent teeth and tendency to early caries were frequent findings.

Various explanations have been offered to account for these facts. Swan *et al.* (1943) believe that the embryonic cells are more susceptible to virus infections than the adult tissues because they are relatively less differentiated. The actual pathological effect of rubella will therefore depend on the period of gestation at which it is operative, and Swan *et al.* state that the average time for the development of cataract is 1.5 months in contradistinction to that for deaf-mutism, which is 2.1 months. Weston Hurst (1943) explains the association of congenital heart disease and cataract in the same child by assuming that the action of the virus is primarily on vascular structure and that in cataract, for instance, it operates on the hyaloid artery, thus interfering with nutrition of the lens fibres. Brown (1947) believes that there may be a direct effect of the virus on the lens *anlage*, or that insufficient adrenal cortical control may account for most of the malformations.

Some doubt has been thrown on the validity of the general hypothesis by Fox and Bortin (1946), who investigated the outbreaks of rubella in 1942-44 in Milwaukee, a city of over half a million. Their figures were :

	1942.	1943.	1944.
Total number of cases	3,998	17,703	525
„ „ in married women	73	477	31
„ „ of married women investigated	19	122	10
Number of babies born to these women	1	9	1

Five of the mothers had rubella in the first two months, 4 in the 2nd-4th month, and 1 each in the 7th-9th month of pregnancy. "Although one mother who had rubella at the end of the first month of pregnancy was delivered of a hydrocephalic stillborn baby, there was not a single example of congenital deformity amongst the 11 babies," and one mother who contracted rubella in the second month produced a normal baby, whereas in a previous pregnancy her baby had bilateral cataract. An investigation in Boston, however, was confirmatory of previous reports (Ober *et al.*, 1947).

A few examples of the effects of other maternal infectious disease on the embryo have been cited, (Laforet and Lynch, 1947), but Fox *et al.* (1948) have summarized their extensive research thus : "One congenital anomaly (hare-lip) occurred in 33 live children born to mothers who had had measles, mumps or chickenpox during pregnancy. For poliomyelitis in pregnancy the overall incidence for anomalies is about twice the expected rate, and in the first four months, nine times the normal rate." "The reports of other workers on anomalies following maternal rubella in pregnancy indicate an overall incidence about 15 times the expected rate of 0.9 per cent., and in the case of mothers who had had rubella in the first 4 months of gestation more than 18 times the expected rate." Swan (1947) sums up the position : "On the available evidence when a woman contracts rubella within the first two months of pregnancy, it would appear that the chances of her giving birth to a congenitally defective

child are in the region of 100 per cent., and if she contracts rubella in the third month they are about 50 per cent. There is still a slight likelihood that the child will be congenitally defective if rubella is contracted after the third month of pregnancy." Suggestions as to prophylaxis and treatment include termination of pregnancy, more rigorous isolation against infections in pregnancy, less rigorous isolation against infections in early life (Erickson, 1944; Greenfield, 1945) and the use of adult serum or gamma globulin.

MONGOLISM.

Among 98 mongols, Engler (1944) found 12 definite cases where miscarriage in the mother due to abortifacients, curettage, or miscarriage of unknown origin immediately preceded the birth of a mongol. He (1945) believes the unhealthy condition of the mucous membrane at the time of implantation of the impregnated ovum to be the chief cause of the condition, and adds data about the age of the mother, 70 per cent. being over 35 years old at the time of the child's birth.

Benda *et al.* (1943) discount the hereditary theory on the ground that mongolism shows no tendency to increase in proportion to the number of offspring in accordance with Mendelian expectation. They attach considerable significance to the birth order of the mongoloid patients, of whose brothers and sisters 84 per cent. were born before the mongol and only 16 per cent. afterwards. If the condition were due to germinal variation the normal expectation would be 50 per cent. born before and 50 per cent. afterwards. They suggest that the results indicate the development of a pathological condition of the mother, as evidenced by the occurrence of mongol births: (1) at the end of the child-bearing period, (2) at the beginning of the child-bearing period and (3) in the middle, due to intercurrent extrinsic factors. The common denominator is the threshold of sterility due to hormonal imbalance, manifesting itself in abortions, bleedings during pregnancy, prematurity and incapacity for conception.

On the basis of studies on 38 cases coming to autopsy, Benda (1942) concludes that the condition follows a pathological gestation (due to a deficiency of corpus luteum—*cf.* Penrose (1932)), which results in a poorly functioning pituitary. Thyrotropic, adrenotropic and gonadotropic stimulation is thus inadequate for the developmental needs of early infancy.

Beidleman (1945) estimates that mongolism occurs in 3.4 per 1,000 births at a large maternity hospital. Bleyer (1942) gives the incidence in the United States as 1 in 4,300 births, and estimates that mongols comprise 14.6 per cent. of all defectives. The condition is commoner in males than females (in the ratio of 62 to 38) and commoner in the city than in the country.

The physical distinction of the disease exists as early as the third or fourth month of foetal life.

Ingalls (1947) ingeniously suggests that the occurrence of the foetal injury can be fixed between the sixth and ninth weeks, as at this time the cartilaginous skeleton of the foetal fingers has been completed save for the laying down of the middle phalanx of the fifth finger, which in the mongol is so frequently malformed.

The comparison is made with foetal abnormalities found after maternal rubella (Ingalls, 1947a).

Some evidence for hereditary predisposition is offered by Turpin *et al.* (1947) in that the fissured tongue is significantly more frequent among the fathers, mothers and cousins of mongols than among controls, and significant differences were found with regard to the simple transverse palmar fold among mongols and relatives and controls (in the ratio of 58.5 per cent. : 9 per cent. : 0.87 per cent. respectively).

Gordon (1946) points out that, since mongols are slow learners, the prognosis as regards mental development need not be so gloomy as is usually thought. Many of them can be taught to read, write, count, tell the time, do simple knitting or crochet work, paint simple subjects from copy and do basketry or other work in the shops. Pototzky and Grigg (1942) found the mean I.Q. in 21 patients to be 46, 11 of whom had mental ages of over 6, and 2 of whom were of border-line intelligence. The average mental age with C.A. of 16 or more was 6.10, and the S.A. (social age) tended to be higher. The writers propose that the terms "mongol" and "mongoloid" should be used to differentiate between those of idiot grade and higher grades.

Benda (1947) suggests that as no suitable pituitary anterior lobe substitute is at present available, the most effective form of treatment is to give thyrotropic hormone $1\frac{1}{2}$ c.c. twice weekly after the first year, though experimentation under X-ray control and metabolism tests may be needed to find the right dose. Thyroid ext. sic. gr. $\frac{1}{10}$ every second day may be given to a child of two months, and at six months it may be given daily. In the second year it may be increased to $\frac{1}{2}$ gr. daily, and from 2 to 4 years the optimal dose does not usually exceed $\frac{3}{4}$ gr. daily. Feeding should be rich in carbohydrates and salts, and low in fats, with frequent small meals.

According to Bixby and Benda (1944), male gonad deficiency leads to lowering of androgen excretion (*cf.* also Benda and Bixby, 1947).

CRETINISM.

Dunn (1944) is of the opinion that many cases of cretinism are secondary to a deficiency of the thyrotropic hormone due to primary anterior pituitary disease. It is important to distinguish these cases from primary thyroid deficiency because they respond to the oral administration of anterior pituitary extract combined with thyroid in low dosage. The differential diagnosis may be helped by finding a very much enlarged sella turcica with extensive osseous retardation. Man *et al.* (1947) have noted a distinct decrease in the serum precipitable iodines in cretinism, which may prove to be useful in diagnosis and the regulation of treatment. Woolley and McCammon (1945) have discussed the changes in bone-growth that follow from thyroid treatment. Bruch and McCune (1944) note that excessive thyroid treatment in an attempt to force the pace, only leads to emotional upsets that interfere with intellectual performance.

RARE SYNDROMES.

Originally described by Shereshevski in 1925, Turner's syndrome, which includes infantilism, mental defect, congenital webbed neck, and cubitus

valgus, has been the subject of further papers by Schneider and McCullagh (1943) and Shereshevski (1944). Gonadal hypoplasia and decreased excretion of 17-ketosteroids are associated features.

Hemihypertrophy of the body according to Ward and Lerner (1947), is associated in 15-20 per cent. of the cases with mental deficiency.

The range of hypertrophy varies from overgrowth of a digit to complete hemihypertrophy, or it may even affect more than half the body. It may involve an extremity, half of the skull, or half the thorax. The right side is more frequently affected than the left, and the hair, pupil, vessels, muscles, interstitial tissues of nerves, and bones may be implicated.

Associated anomalies include naevi, telangiectasia, macrodactyly, syndactyly, polydactyly, abnormal nail growth, premature eruption of the teeth, excessive sweat and sebaceous secretion, pigmentation of the skin, supernumerary nipples, congenital heart disease, scoliosis, tilted pelvis, clubbed feet, hypospadias and cryptorchidism.

Over 100 cases have been reported (Schwartzman *et al.*, 1942), and its association with von Recklinghausen's disease has been noted by Huse (1944). Van Bogaert and Kegels (1947) described a case as the Klippel-Trenaunay syndrome, while Parkes Weber (1943) has spoken of the condition as haemangiectatic hypertrophy of the limbs (Klippel-Weber, or Weber-Klippel syndrome). The condition should be differentiated from hemiatrophy following birth injury, as from a lesion of the post-central cerebral cortex.

Other naevoid conditions associated with mental deficiency have been reported (Weber, 1946), while Worster-Drought (1948) has reported a case of the Sturge-Kalischer-Weber syndrome of bilateral distribution. He quotes Parkes Weber's view that the cause is accidental local injury to the embryo.

BIRTH INJURY.

McIntire (1946) considers that the most probable cause of cerebral palsy is birth injury, using the term in its broadest sense, to include not only mechanical damage inflicted during the birth process, but any other intracranial damage occurring just prior to, during, or immediately following birth.

Of 500 patients with cerebral palsy, 50 per cent. were attributed to birth injury, 23 per cent. to intracranial congenital defect, birth injury or intracranial congenital defect in 8 per cent., post-natal injury in 5 per cent., encephalitis in 4 per cent. and other causes 10 per cent. Fifty-eight per cent. occurred in males, 42 per cent. in females. Four per cent. were of superior intelligence, 8.8 per cent. high average, 25 per cent. average 7.6 per cent. low average, 11 per cent. dull normal, 5.8 per cent. border-line, 27.6 per cent. feeble-minded, 10.2 per cent. undetermined.

Speech defects were present in 54.6 per cent., 15 per cent. having no speech.

The distribution of the types of physical handicap were assessed as follows: Spasticity 44.8 per cent., athetosis 33 per cent., tremor 7 per cent., rigidity 2.6 per cent., primary inco-ordination 4.6 per cent., mixed spasticity and athetosis 2.6 per cent., other combinations 5.4 per cent. The extent of the physical handicaps was as follows: Quadriplegias 56.6 per cent., triplegias 6 per cent., hemiplegias 25.6 per cent., diplegias 9 per cent., monoplegias 1.6 per cent., all others 1.2 per cent.

Stewart (1942) supports Collier's view (1924) that the essential cause of all cases of diplegia is primary neuronal degeneration, though he allows the possibility that anoxaemia and nutritional deficiencies may be important etiological factors.

Yannet (1944) in a study of 86 patients with cerebral palsy concluded that developmental cerebral malformation, in some cases due to genetic causes, might be the most likely etiological explanation, though admitting that in 25 per cent. of the cases there was a history of abnormal labour, including breech presentations, difficult forceps deliveries, and prolonged labour with difficulty in resuscitation of the infant, and that 12 per cent. of the patients were born prematurely, in contrast to the usual incidence of 4-6 per cent.

McGovern and Yannet (1947) investigated 67 cases of asymmetrical spastic infantile cerebral palsies, and concluded that the etiological factors were distributed as follows: Birth trauma 12, post-infections 11, Rh factor 7, neon-plasm 1, undifferentiated 36. This last group tended to be associated with advanced maternal age and prematurity.

Wyllie (1948) noted that abnormal labour is an important etiological factor in 23 per cent. of cases of infantile hemiplegia, but defines two main pathological forms, a non-specific acute toxic encephalopathy, and a haemorrhagic variety. He also refers to the occurrence of acute infectious diseases in one third of the cases.

Stewart (1948) in 112 cases of infantile hemiplegia described two main types: (a) The congenital (50 cases), 26 being due to difficult or abnormal labour, 10 to ill health of mother during pregnancy, 2 to injury to mother by fall during pregnancy, 2 to cerebral angioma with facial naevus, and 10 to unascertained causes; and (b) the acquired (62 cases), 9 attributed to syphilis, 7 to encephalitis, 6 to meningitis, 5 to whooping-cough, measles and scarlatina, 4 to head injury, 3 to vaccinia, 2 to tuberosc sclerosis, and 26 to unascertained causes.

Christensen and Schondel (1946) point out that porencephaly and poly-porencephaly occur most commonly in premature infants and that these children are more liable to birth injury, which is followed by haemorrhage and circulatory disturbance.

The relationship of prematurity to birth injury and mental deficiency is reviewed by Asher (1946).

Some confirmation as to the importance of intracranial injury and asphyxia in the death rate of the premature is afforded by Agnes MacGregor's (1946) figures based on post-mortem studies of 345 cases of still-birth, and 618 neonatal deaths, of whom 24.1 per cent. and 27.6 per cent. respectively were found to have died from intracranial haemorrhage, and 37.2 per cent. and 13.1 per cent. respectively from asphyxia. Among the live-born infants dying of asphyxia 82.7 per cent. were premature, and of those dying from intracranial haemorrhage 81.8 per cent. McNeil *et al.* (1947) confirm the importance of intracranial birth injury as a cause of death in the premature.

In 200 consecutive post-mortems, Bender (1947) attributed mental defect to vascular accidents and birth injury in 38 cases.

Lamm (1943) believes that the important factor in the causation of brain-injury is asphyxia, quoting Schrieber (1940) for the opinion that in 900 children whose brain defects were thought to be related to conditions at birth, 70 per cent. had a history of asphyxia. He defines four different kinds, anoxic anoxia due to failure of ventilation as from obstruction of the air passages, stagnant anoxia resulting from slowing of the circulation, anaemic anoxia due to haemorrhage, anaemia, or following drug therapy, and histotoxic anoxia, from failure of cells to use oxygen, as from anaesthetics. Prematurity is the most important single factor in the etiology of neonatal asphyxia.

This view widens the whole approach to the problem of birth injury and is capable of explaining not merely the gross cases of cerebral palsy, but also the not inconsiderable group of hyperkinetic, epileptic, and apathetic cases described by Preston (1945). Nielsen (1946) is of the opinion that birth difficulties are a major cause of idiopathic epilepsy, and Bonner (1947) ascribes 22·8 per cent. of cases to birth and neonatal injuries.

In a total of 132 cases Preston identified behaviour disorders due to prenatal, natal, or post-natal anoxia in 81 males as against 51 girls, in the total of which 35, or 26 per cent., were of subnormal intelligence (19 morons, 14 imbeciles and 2 idiots). In this subnormal group, 9 were hyperactive, 14 epileptic, 7 apathetic and 5 unclassified. The importance of prophylaxis is stressed, especially in the abuse of analgesics and anaesthetics.

The clinical picture included various grades of neuromuscular inco-ordination, from tremors and twitchings to athetosis and spasticity, motor restlessness, impulsiveness, lethargy, distractibility, defective speech, uncontrollable temper, inability to concentrate, gradually increasing scholastic retardation, destructiveness, extreme jealousy, cruelty, aggressiveness and apathy.

The devastating effects of this behaviour on the family and on the child's capacity for making social contacts are indicated, and although some degree of recovery is usual, this occurs only after a considerable amount of time has been lost at the expense of general educational progress.

Malamud and Haymaker (1947) described three cases of head injury in which the lesions were in the lenticular nuclei, and suggested that anoxia may be the basis of cases of post-traumatic Parkinsonism.

Faber (1947) made a study of the etiological factors present in 99 cases of cerebral cortical atrophy, all of which had been confirmed by pneumoencephalography, with special reference to the anoxic factor. Mental deficiency was present in 74 per cent., spastic paralysis in 43 per cent. and convulsive states in 48 per cent. He noted that when he tried to classify episodes suggestive of damage occurring in the prenatal, the paranatal, or the post-natal periods, in 26 cases there was a history of episodes in more than one period, but in terms of the period in which the probable causative factors were operative, the respective figures were, prenatal 35 per cent., paranatal 40 per cent. and post-natal 25 per cent.

Among the prenatal factors were placental separation, toxæmia, oversized infant, premature rupture of membranes, maternal trauma, Rh incompatibility, premature labour, attempted abortion, maternal cardiac decompensation, and maternal infectious diseases.

Among the paranatal factors were anaesthetics, sedation, induced labour, breech presentations, abnormal deliveries and abnormalities of the cord.

Of the post-natal factors, infections of various kinds were the most important, but a few were attributed to severe convulsions of unknown cause, and to cerebral trauma.

His conclusion is that "better obstetrics and better paediatrics could have prevented a considerable part of these disasters merely if the present-day knowledge had been applied."

Pathological confirmation of the widespread effects of neonatal asphyxia is given by Courville and Marsh (1945).

An extremely interesting account of the experimental evidence of the importance of anoxia is provided by Windle and Becker (1943).

The problem of cerebral palsy.—Applying Phelps's principles to the treatment of sufferers from cerebral palsy, Collis and Buck (1946) report the measures taken to assess the degree of handicap: (1) Functional ability; (2) nutrition and appearance; (3) aetiology and final diagnosis; (4) classification of 5 motor groups—spastic, athetoid, ataxic, rigidity and tremor; (5) spastic disabilities—example, muscle imbalance, joint motion difficulty, eye defects, hearing defects; (6) dominant handedness; (7) mentality, having regard to sensory motor handicap assessment and former environmental factors. Training includes (a) physiotherapy, which embraces respiratory and deglutition difficulties; relaxation; discipline; rest; correction of faulty habits, especially of correct motor patterns; balance; voluntary postural correction and special sense training. (b) Activities, for example, hopping, ball throwing, rhythm and group work. (c) Occupational therapy. (d) Speech therapy. (e) School-work.

Evans (1946) concludes that in order to obtain the optimum results in dealing with children suffering from cerebral palsy, the following factors should be borne in mind—to differentiate athetoid quadriplegics with tension from those suffering from spastic disorders; to include those patients who are ineducable; to begin treatment early; to confine operative treatment to the realms of structural contractures in spastic cases; to exclude epileptics; to secure co-ordination of effort between physiotherapist, occupational therapist, speech trainer, school teacher, psychologist and medical personnel; to establish a number of residential remedial schools where treatment can be instituted from physical and mental aspects in order that they may proceed to a steady degree of rehabilitation, so that they may profit from education.

According to Frantz (1946) 7 children with cerebral palsy out of a population of 100,000 will be born every year; one of these will die before reaching the age of 6 years, 2 will be feeble-minded and 4 will be in some measure amenable to treatment. So that in a community of 100,000 population there would be, under the age of 16 years, 50 to 60 subjects falling into the third category. Of the cases so treated he estimates that 28 per cent. are severely affected, 44 per cent. moderately affected and 28 per cent. mildly affected. He concludes that the spastic child is mentally and physically a different kind of person and forms a special entity.

Leden and Krusen (1947) stress the importance of relaxation in the treatment of the athetoid, whose muscles they believe to be essentially normal. The child is taught how it feels to relax completely and how to eliminate tension in each muscle. Relaxation is not of such great value in the spastic child. Carlson (1946) considers that the first object in treating the patient is to educate his muscles until control is obtained. The brain at birth is unable to select sensory impressions and translate them into compulsive action, and until this capacity is developed the normal child grimaces and exhibits muscular rigidity suggestive of mild spastic and athetoid conditions. These aimless movements cease as the cortex develops and concentration of performance is achieved. Along with this the effect of education on the emotions is important because through control of the emotions the cerebral palsied learn to control muscular movements.

Collis (1947) estimates the incidence of athetoids to spastics as in the ratio of 5 to 1. No true cases of ataxia were discovered, though doubtful ones are often found to have athetosis. Spastic conditions are believed to be pyramidal in origin and athetoids extrapyramidal, while dual lesions are rare. The important point is stressed that children regarded as defective because of hospital treatment or motor disability, by rehabilitation have been enabled to catch up to normal.

Leden and Krusen (1947) state that one of the greatest obstacles to advancement in treatment has been the general opinion that a cerebral birth injury is almost always associated with mental deficiency. They cite as the three commonest causes of the condition congenital maldevelopment, birth injuries and encephalitis. Less than 50 per cent. of affected children have had a difficult birth and less than 3 per cent. were due to poor obstetrical care. The two main types to be distinguished are the athetoids and the spastics and the distinguishing features are summarized as follows :

	Athetoid.	Spastic.
Site of lesion	Extrapyramidal	Pyramidal.
Temperament	Extravert.	Introvert.
	Little fear.	Fearful.
	Prolonged fits of anger	Anger rare and short-lived.
Rigidity	Due to superimposition of involuntary motion on voluntary.	Evoked by minimal stimuli.

Hall and Benda (1947) report disappointing results from the use of prostigmin for the rigidity of cerebral palsy. Jepson (1946) and Pohl (1946) have also given accounts of its use for this type of case.

DEVELOPMENTAL PSYCHIATRY.

Of the most important advances in mental deficiency, the work of Gesell and his associates over the last 35 years must claim prior attention. It is not so much that one can point to individual discoveries, but that by the patient application of a particular attitude to the whole subject, there has

arisen a substantial body of knowledge which in many ways breaks away from the traditional approach to mental deficiency.

Gesell and Amatruda (1947) have formulated the concept of the developmental quotient (D.Q.) and set up norms to compare the developmental status of any child with the norms appropriate to his age, and to determine whether he deviates from the norms, in what direction he deviates, and how much he deviates.

The D.Q. is the relationship between maturity age and actual age expressed as a percentage.
$$D.Q. = \frac{\text{maturity age}}{C.A.} \times 100.$$
 It expresses the rate of development and the proportion of normal development that is present at any given age. It is the beginning of developmental diagnosis and is applied to four fields of behaviour :

(1) Motor development ; (2) adaptive behaviour ; (3) language ; (4) personal-social development.

Only when the maturity in the several fields is at nearly the same level is it permissible to assign a single inclusive maturity level and a general D.Q. The authors emphasize the importance of using the D.Q. not, as too often the I.Q. is used, as a fixed standard, but as a pointer which may measure the beneficial effects of treatment. It is an indication for further diagnostic refinement, to seek for causes and ways of amelioration.

Gesell (1947) considers that "developmental pediatrics" has a very wide sphere of application, and Amatruda (1942), writing on the value of pneumoencephalography in various cerebral conditions, indicates that the procedure is less informative than the application of Gesell's methods would be.

(Other writers on the value of pneumoencephalography in the differential diagnosis of mental deficiency have been Ross and Dickerson (1943), Delay *et al.* (1947 and 1947a), Levinson (1947), and Bourrat and Gallavardin (1947)).

The differences in the development of different grades of defectives is indicated in the following scheme :

Comparative Development—Normal, Moron, Imbecile and Idiot Behaviour—at 28 Weeks and 3 Years of Age

28 Weeks

Motor Behaviour.

	Maturity level,
Normal : Sits alone, leaning on hands, head erect	28 wk.
Moron : Sits supported, head steady but set forward	12-16 wk.
Imbecile-idiot : Sits supported, head unsteady	8-12 wk.
Low-grade idiot : Head droops	0-4 wk.

Adaptive Behaviour.

Normal : Reaches, grasps, transfers	28 wk.
Moron : Does not reach, regards object in hand	12-16 wk.
Imbecile-idiot : Disregards or only glances at objects in hand	8-12 wk.
Low-grade idiot : Stares vacantly ; may hold object reflexly without regard	0-4 wk.

Language Behaviour.

Normal : Vocalizes "m-m-m"	28 wk.
Moron : Chuckles or laughs aloud	12-16 wk.
Imbecile-idiot : Smiles ; feeble vowel sounds	8-12 wk.
Low-grade idiot : Vague throaty sounds	0-4 wk.

Personal-Social Behaviour.

	Maturity level.
Normal : Takes solids well	28 wk.
Moron : Chokes on solids ; anticipates feeding	12-16 wk.
Imbecile-idiot : Watches moving person	8 wk.
Low-grade idiot : Stares blankly at persons	0-4 wk.

*3 Years**Motor Behaviour.*

	Maturity level.
Normal : Climbs stairs with alternating steps	3 years.
Moron : Walks	18-24 mo.
Imbecile : Stands	40-52 wk.
Idiot : Sits supported, head steady or wobbly	12-16 wk.
Low-grade idiot : Lifts head in prone	0-4 wk.

Adaptive Behaviour.

Normal : Builds bridge from model	3 years
Moron : Builds tower of 2-3 cubes	18-24 mo.
Imbecile : Dangles ring by string	40-52 wk.
Idiot : Grasps object near hand or on contact	16 wk.
Low-grade idiot : Stares vacantly ; drops object in hand	0-4 wk.

Language Behaviour.

Normal : Speaks in sentences, using plurals and prepositions	3 years.
Moron : Names a few pictures	18-24 mo.
Imbecile : Says "mama"	40-52 wk.
Idiot : Laughs	16 wk.
Low-grade idiot : Crying and vague ejaculation	0-4 wk.

Personal-Social Behaviour.

Normal : Feeds self, little spilling	3 years
Moron : Carries and hugs doll	18 mo.
Imbecile : Offers toy to mother	40-52 wk.
Idiot : Anticipates feeding ; smiles on social approach	16 wk.
Low-grade idiot : Stares blankly at persons	0-4 wk.

(*Developmental Diagnosis*, by Gesell and Amatruda, p. 122.)

Discussing the question as to whether infants have I.Q.'s, Irwin (1942) is of the opinion that tests given to infants do not measure intelligence but the structural conditions for its later appearance. Intelligent behaviour therefore depends on the later acquisition of certain anatomical and physiological functions, e.g. the establishment of cortical connections, the control of vision, the ability to stand and walk, and the acquiring of special mechanisms for symbol-representation.

Penfield and Robertson (1943) state that decrease in the growth of one side of the body, or of one member, may result from a lesion of the corresponding portion of the spinal cord at an early age or from a large birth injury of the opposite hemisphere, and therefore that the post-central cerebral cortex has an influence on the growth of the opposite side of the body, with localization approximate to that of cortical sensation.

Thorne (1945), in his developmental studies of pyramidal spasticity, describes four degrees corresponding to the period in which they were initiated :

(a) Symmetrical pyramidal spasticity, suggestive of prenatal maldevelopment (congenital cerebral spastic paralysis), usually generalized with early or later contractures, in which the deformities with signs of upper motor neurone lesions are present at birth. The prognosis is poor because irreversible damage has occurred early in foetal development. Further damage may occur at birth from abnormal presentation.

(b) Asymmetrical pyramidal spasticity is present at birth, or follows trauma to the central nervous system (Little's disease). Focal lesions with slowly developing contractures and varying degrees of mental defect according to the extent of the lesion are characteristic. The prognosis is relatively good with physiotherapy. Two such types may be differentiated: that due to cerebral haemorrhage with extensive motor involvement and that due to asphyxia, with diffuse cortical impairment. Cerebellar and striatal syndromes may be coincident.

(c) Symptomatic pyramidal spasticity comes on after birth, and is post-natal in origin, as from encephalitis, acute illness, cerebral trauma or a convulsion. Normal or diminished motor tone and reflexes may, in a course of months or years, be followed by pyramidal spasticity and contracture deformities. Extrapyramidal signs may be associated.

(d) Pyramidal spasticity may follow neglect from prolonged immobilization, as from a fracture, and especially if the parents are defective. Contracture deformities thus arise from inhibited development of motor function, but it may also be associated with ataxia and hypotonia.

Treatment by relaxation and passive movement therefore is important to maintain complete mobility of function in the affected limb until voluntary control is acquired, or until restraint is removed.

Although the author's general conception is a helpful one, it must be admitted that, clinically, many cases are encountered in which the effects of birth injury are delayed for some months, as, for example, in cases cited by Norman (1947) and Wyllie (1948).

ENCEPHALITIS AND ENCEPHALOPATHY.

The importance of encephalitis of diverse etiology in the production of various conduct disorders is slowly being recognized. Greenebaum and Lurie (1948) have analyzed 78 cases (61 boys and 17 girls) of age-range from 4-19. In 80 per cent. the date of onset was from 5 months to 7 years.

Types.

I. Virus :

1. Polio-encephalitis	.	.	.	.	.	5	} Total, 37.
2. Lethargic encephalitis	.	.	.	.	.	7	
3. Influenzal	„	.	.	.	.	7	
4. Measles	„	.	.	.	.	8	
5. Chickenpox	„	.	.	.	.	1	
6. Unknown origin	.	.	.	.	.	9	

II. Toxic :

1. Diphtheritic encephalitis	.	.	.	.	.	2	} Total, 29.
2. Scarletinal	„	.	.	.	.	2	
3. Pneumonic	„	.	.	.	.	4	
4. Whooping-cough	.	.	.	.	.	15	
5. Meningo-encephalitis	.	.	.	.	.	1	
6. Of unknown origin	.	.	.	.	.	5	

III. Traumatic	.	.	.	.	.	.	Total, 12.
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They describe three main patterns of behaviour disorder—simple, psychopathic and psychotic. Eighteen of the cases had I.Q.'s. of 70 or less, and neurological abnormalities were noted in all but 21 of them. These comprised signs of pyramidal disease (38), extra-pyramidal (20), ocular (16), attacks of *petit mal* (3) and attacks of *grand mal* (6) (*cf.* Fairweather, 1947).

Levy and Perry (1948) found among a group of 128 children who gave a positive history of whooping-cough prior to admission, that 20, or 15.6 per cent., became intellectually retarded as a direct consequence. They confirm that the younger the age when whooping-cough occurs the greater the damage.

Thus, of those who had whooping-cough between birth and 2 years of age the incidence for intellectual retardation was 29.2 per cent. Between 2 and 5 years the incidence was only 14.3 per cent., and after this age the incidence was only 2.2 per cent.

One of the most striking and characteristic findings was a history of delay or relapse in regard to walking and talking. One of 19 children who walked and talked before the attack experienced immediate arrest of these faculties following the attack. Considerable time elapsed before they could resume these functions. They noted in a large number, positive neurological findings, pyramidal and extrapyramidal signs, speech defects and nerve deafness. Eight were classified as idiots, 8 as imbeciles and 4 as low-grade morons. Some of the children also showed various forms of psychopathic behaviour.

Frank (1947) considers that the neurological effects of whooping-cough may be due to intracranial haemorrhage, spasmophilic tetany, serous meningitis, meningismus, encephalitis or encephalosis. The author quotes Spatz and Husler (1924) for the view that encephalitis associated with whooping-cough is not encephalitis within the strict meaning of the term, the degenerative necrobiotic alterations found at autopsy being chiefly consequences of circulatory disturbances similar to those seen as a result of lead poisoning. Mark (1947) considers that they are due to anoxaemia and that the term encephalopathy is preferable. In view of the occasional sequel of mental deficiency following prophylactic injections for whooping-cough or diphtheria, interest is attached to the reports by Brody (1947), and Brody and Sorley (1947) on the neurological complications resulting from the administration of pertussis vaccine. In one case the clinical picture was that of a demyelinating disease of the central nervous system (hypotonia, somnolence, dysemia and constipation followed by hemiplegia and mental deterioration), and in another, that of a lesion in the cortical grey matter, as evidenced by pneumoencephalogram, mental deterioration and generalized convulsions. In both conditions neurological sequelae quickly followed an injection of vaccine and recurred with greater severity when the dose was repeated.

Bruetsch (1947, 1947a) has described the late sequels of rheumatic fever and notes that the type of mental disturbance is determined by the personality and the age at which the cerebral involvement occurs. The aberrations range from mild behaviour disorders to slight mental deficiency states. In young adults states suggesting dementia praecox have been observed (Warren and Chornyak, 1947). Leys (1946) has described three cases of rheumatic encephalo-

pathy which occurred when there was an increased prevalence of non-specific meningoencephalitis in the district.

Pai (1946) has recounted 29 patients with residual neuropsychiatric symptoms after cerebrospinal fever in early life. The majority showed personality defects and complained of symptoms suggestive of an encephalopathy. They were backward at school and found difficulty in adaptation both at school and later at work.

Organic defect syndromes have also been noted after cerebral malaria (Irish, 1946; Boshes, 1947).

Bender (1943) has described seven cases of burn encephalopathy in children. The condition appears to be a secondary pyogenic infection and leads to psychopathic behaviour which attains its maximum at puberty. The original trauma occurred in all cases in early childhood, and gave rise to three main groups of symptoms:

(1) Neurological: Oculo-motor disturbances (unequal or irregular pupils, nystagmus), lack of facial expression, mimicry, deficient associated movements, choreiform movements, tics, convergence of outstretched hands and interference with postural reflexes, e.g. gyration.

(2) Specific intellectual disabilities, e.g. of gestalt formation, with difficulties in integrating perceptual experiences involving visuo-spatial relationships, tested for by Kohs' blocks, Goodenough drawing of a man, and weight differentiation.

(3) Behaviour: Hyperkinesis involving extrapyramidal motility, especially manifested in an illusive search for objective reality, e.g. touching, taking, destroying, abusing, nagging, over-loving and clinging.

Lurie *et al.* (1947) believe that the diagnosis of a post-encephalitic state can be made on the characteristic behaviour and personality changes even in the absence of definite history or neurological findings, but that the prognosis remains poor and appears to be worse in those with toxic or traumatic infections.

Bender (1942) states that the diagnostic criteria for encephalopathic behaviour disorders are now considerable. Even without a history of the specific etiological factor or evidence of the specific pathology, the diagnostic methods which may be applied to fields of behaviour are sufficient to establish a diagnosis.

Three unusual cases of encephalitis not fitting easily into recognized types are dealt with by Rosonoff (1947). They have in common an insidious onset, a subacute or chronic course, and a rather diffuse spread of lesions throughout grey and white matter. One case closely resembled the "leuco-encéphalite sclérosante subaiguë" of Van Bogaert (1945).

Toxoplasmosis has been recognized only since 1939 (Wolf *et al.*), but increasing numbers of cases are being reported, and the first case in this country is described by Jacoby and Sagorin (1948). The congenital type may be present at birth or the symptoms may not appear until several months later. Hydrocephalus is one of the commoner manifestations, but microcephaly has appeared in some cases. Convulsions, mental changes, "scissors" position of the lower limbs and deviation of the head, chorio-retinitis with subsequent optic atrophy, and cerebral calcification in the basal ganglia or the optic thalamus, appearing

in radiographs as curvilinear streaks, form a fairly typical clinical picture. A test has been devised by Sabin and Rushman (1942) to demonstrate neutralizing antibodies in the serum. Demonstration of the protozoon toxoplasma is usually only possible after death. Animals, either directly or through insect vectors, appear to be responsible for the human infection.

Because of the occurrence of the condition in post-encephalitics, considerable interest is attached to the paper by Critchley and Hoffman (1942) on the Kleine-Levin syndrome, characterized by periodic somnolence and morbid hunger, originally described by Kleine (1925) and Levin (1929, 1936 and 1938). Ronald (1946) has reported two additional cases.

Byers and Lord (1943) made a study of the late effects of lead poisoning on mental development in 20 cases, and concluded that extreme difficulty in adjustment in both intellectual and emotional spheres was a typical sequel.

Thorpe (1946) recorded beneficial results after prefrontal leucotomy in post-encephalitics with disorders of conduct. Mackay (1948) gave an account of the effects of this operation in 20 psychopathic feeble-minded patients at Rampton State Institution, of whom 7 showed such marked improvement as to deserve consideration for discharge, 7 were improved, 5 showed little or no change, and 1 died.

Engler (1948) described the effects of the operation on 44 mental defectives and concluded that on the whole the results were disappointing. The operation should be performed only on defectives with a higher degree of intelligence and a higher standard of personality.

GLUTAMIC ACID AND NUTRITIONAL FACTORS.

Zimmerman and Ross (1944) discovered that *glutamic acid* given to rats increased their powers of maze-learning. Zimmerman *et al.* (1946) later reported an experiment in which glutamic acid was fed to 9 children, of whom 7 were epileptic and 2 mentally retarded. The dose varied from 6–24 gm. a day and was maintained for six months. In every one of the epileptic children there was clinical improvement—5 of the 7 ceasing to have fits, though phenobarbitone was also given. Apart from the two youngest children the remainder showed a greater improvement in intelligence than could be expected from lapse of time alone, and the I.Q. rose 5–13 points, with an average of 9. Zimmerman *et al.* (1947) suggest that this is a rate of development twice that of normal children and favours a more flexible definition of intelligence than has often been employed in psychological literature.

Price *et al.* (1943) also report the effect of *dl*-glutamic acid hydrochloride in *petit mal* and psychomotor seizures.

Albert *et al.* (1946) compared the effect of *dl*-glutamic acid hydrochloride with that of the naturally occurring form and show that the latter is as effective as the racemic variety. The chronological age of the 8 patients studied, all of whom had secondary mental deficiency, ranged from 6 to 26, mental age from 2 to 8 and I.Q. from 22 to 73. In 7 of the 8 patients an unmistakable rise occurred as a result of treatment, and on placebos they slumped back to the previous level of performance, but improved again when placed back on glutamic acid. The effect was to make the patients more alert, attentive and

persistent in trying to accomplish the tasks put before them. Emotional regulation also appeared to improve. They make the suggestion that the effect appears to be to release neural mechanisms.

Other research indicates that glutamic acid may shorten the period of confusion and memory impairment following the shock treatment of psychotic patients.

Goodman *et al.* (1946) experimented with glutamic acid in the electrically produced convulsions on animals. They report that it showed neither anti-convulsant nor analeptic action. It had no effect on the EEG changes, unlike the other drugs tested, and the writers conclude that if this fact is substantiated its mode of action must be very different from that of known anti-convulsant drugs.

Nachmansohn *et al.* (1943) found that *l*(plus)-glutamic acid added to extracts of rat brain increased the rate of formation of acetylcholine about 4-5 times. They asked the question, therefore, whether it is a co-enzyme of choline acetylase.

Zimmerman *et al.* (1948) present a report on the first 30 cases completing a full year on glutamic acid therapy. The group comprised children and adolescents with convulsive disorders, of whom 7 were mentally retarded and 16 were mentally retarded without convulsions. The intelligence quotient gained over the year ranged from zero to 17 points, with an average gain of approximately 11 points, or 24 months, which is twice as much as that expected of children with average intelligence. The authors conclude that the acceleration is general and is not restricted to segments of the intelligence and personality of the individual. The greatest improvement in intelligence and performance occurred within the initial six months of treatment, after which the acceleration diminished and appeared to be approaching a ceiling after one year of therapy.

The effect of added *thiamine* on learning was investigated by Ruth Harrell (1943). Seventy-four orphanage children ranging in age from 4 to 20 years were divided into two groups as similar as possible in heredity, sex, age and intelligence, etc. One group received 2 mgm. extra thiamine daily, the other a placebo, while the daily content of thiamine in the orphanage diet was estimated at 0.9 mg. The two groups were found to be initially well-matched in the performance of the various tests given, which included addition, subtraction, multiplication, division, problems, completing designs, reading, throwing and strength of grip in both hands. At the end of the experiment the thiamine group was found to have made superior gains in every one of the 18 tests, the superiority varying from 7 to 87 per cent. among the various tasks. The average superiority and improvement of the thiamine group over the control group was about 27 per cent.

Guetzkow and Brozek (1946) applied a number of tests to 8 normal young men exposed for 161 days to a diet restricted in vitamin B. This was followed by an almost total deprivation for 23 days. The authors found that there was no intellectual deterioration from the partially restricted diet, but that acute deprivation of the B complex did result in limited deterioration of intellectual functions and that speech appeared to be most affected. It was noted that during the acute deficiency a marked reduction in spontaneous activities,

such as reading books, writing letters, study and conversations, occurred. There was also a noticeable lethargy. Any intellectual impairment that was observed recovered upon a 10 days' liberal supplementation with thiamine alone. In cases of general malnutrition the sensory function appeared to be more involved than the motor functions, which Stannus (1948) attributes to anoxia as the sensory nuclei consume far more oxygen than the motor nuclei. The author assumes the basic deficiency to be one of riboflavine, which causes a hold-up in the normal breakdown of glucose, which is the sole source of brain energy. According to Hailman (1944) riboflavine increases the resistance of nervous tissue to anoxia.

Kugelmass *et al.* (1944) studied the effects of malnutrition on mental development. Two groups of children between the ages of 2 and 9, comprising 50 mentally normal and 41 retarded in each group, of whom the first were all suffering from malnutrition at the time of the test, and who were well nourished at the date of the second test. Among the initially malnourished there was an average rise of 10 points of I.Q. and 18 points for the mentally normal. The control group showed no change. The younger the malnourished children the greater the chance of improvement in mental function. The sharp decline in average rise in I.Q. for the malnourished children who had passed the age of 4 suggests that irreparable damage is to be expected as the children grow older.

Three and a half years elapsed between the tests in the retarded children and two years between the test in the normal.

Kugelmass (1943) shows that a striking feature of the mentally normal malnourished group was a spontaneous alleviation of nervous symptoms with improvement in nutrition. The children became more interested, attentive and responsive, and showed greater ability to concentrate upon their school tasks. Many nervous manifestations, such as tics, nail-biting, fidgeting, fretfulness, sleeplessness, bed-wetting, night terrors, diminished but did not clear during the course of these observations.

THE SOCIAL ASPECTS OF MENTAL DEFICIENCY.

Esher (1942) points out that intellectual subnormality is not the same thing as mental deficiency, the former relates to what the academic psychologist tries to measure by tests, and the latter to the patient's social capacity. MacCalman (1942) says that men have been found with mental ages as low as five years, working as boiler-cleaners, agricultural labourers or painters. Their apparent stability is due to good family training and influence, sympathetic education and the good offices of wives, employers and neighbours. Similarly, Pearson (1945) suggests that high grade imbecile females may give better satisfaction in domestic situations than high grade feeble-minded females with unstable tendencies. MacCalman contends that there is something seriously wrong with our whole approach to the education of the defective when only about 15 per cent. of defective children are educated in a special school, many of whom are not sent there until they are between 10 and 12 years old, or when only 0.2 per cent. of the population is under statutory supervision when about 5 per cent. of the army intake is of an equivalent intellectual standard.

A number of different problems are involved in these observations which are related to (1) the conception of social incompetence in contrast to that of mere intellectual retardation; (2) types of education suitable for different kinds of intellectual defect; and (3) the nature and treatment of disorders of behaviour associated with mental deficiency.

Doll (1947*a*), noting the serious difference in educational objective for those who will always be feeble-minded and in need of some social assistance and supervision, as apart from those who are merely intellectually retarded, suggests that the former group should be directed towards the inculcation of habits and virtues which will minimize the social consequences of their dependency, while encouraging maximum initiative and resource for those who will be socially self-directing and self-supporting.

The matter of differential diagnosis therefore becomes all-important because the one is relatively incurable, while the other is remediable. He believes that in order to make this distinction it is necessary to use a battery of tests which will include a group test, individual tests, verbal and non-verbal tests and performance tests.

Doll (1947) says that true feeble-mindedness, which is incurable, must be differentiated from pseudo-feeble-mindedness which it sometimes simulates. This condition is mere intellectual retardation. The important differentiae are the presence in the former case of evidences of social incompetence, defects of physical development and signs of somatic inferiority, while the latter is largely constituted by reading disabilities, language handicaps and sensory and motor limitations. Grace Arthur (1947) has described five types of pseudo-feeble-mindedness: (1) Individuals with special disabilities, compared with poor general ability; (2) individuals with delayed speech, not preventing the development of non-verbal abilities; (3) individuals who had suffered severe early illness that delayed but did not prevent mental development; (4) individuals with brain injury, e.g. birth, or post-natal trauma which interfered with some kinds of intellectual activity; (5) individuals with special physical handicaps, e.g. impaired vision or hearing, or congenital word deafness. Doll (1947*a*) draws attention to the fact that there has been a swing of emphasis in recent times from nature to nurture, which raises the whole question as to the desirability of institutional treatment in mental deficiency; and Gesell and Amatruda (1947) have actually defined the clinical picture that follows the retardation due to upbringing in an institution, the main effects of which are due to impersonalization and lack of intimate family life. Whitney (1945) affirms that special-school children giving promise of social adjustment call for a complete investigation, with trial periods to ascertain their latent capacities before ultimately placing them in a work situation; "a simple Binet test is no longer an adequate psychological study. It needs supplementation and confirmation by a battery of other manual, verbal and non-verbal tests of measurement."

Blackburn (1948) sounds a note of caution against accepting tests for measuring intelligence for job-selection. Similarly, Marshall (1942) points out the danger of allowing isolated mental tests to dictate educational policy. She points out that some maladjustment may be due to the fact that the school

work given is not appropriate to the pupil's abilities because it is below his level of achievement.

Steeles (1942) has made a study of the effects of differential stimulation on mentally retarded children. The experimental group included 13 retarded children from the Iowa Soldiers' Orphans Home (a relatively non-stimulating environment) who were transferred to the Glenwood State School (a relatively more stimulating environment). The children were all under the age of 3 at the time of transfer. The mean C.A. was 19.4 months, with a range from 7.1 to 35.9 months. The mean I.Q. was 64.3, with a range from 35 to 89. The contrast group which acted as controls were 12 children in an orphanage nursery, with a mean C.A. of 16.6 months (range 11.9 to 21.8 months), and mean I.Q. of 86.7 (range 81 to 103).

A follow-up study was made 2 to 3 years after the close of the experimental period and results were summarized: (1) The level of intelligence of the experimental group had markedly increased, while that of the contrast group showed an equivalent loss; (2) 11 of the 13 experimental children attained normal, or above average, intelligence, and were placed in adoptive homes. Two and a half years later these children had maintained and augmented the earlier gains in intelligence; (3) children in the contrast group, with some variation, had maintained their marked degree of retardation; (4) a change from marked mental retardation to normal intelligence in children of pre-school age is possible by providing suitable domestic care; (5) children of normal intelligence may become mentally retarded to such a degree as to require permanent institutionalization under the continual adverse influence of a non-stimulating environment.

Simonsen (1947) made a comparison of the mental development of normal children with that of children reared in children's homes and day nurseries. The children brought up under institutional conditions were found to yield an average score by Bühler-Hetzer tests 8 points lower than that of the other children. The explanation given for this was that these children showed less than average productivity. Shapiro (1947) found that 5 apparently mentally retarded infants from institutions showed improvement after being provided with a mother substitute. Individual nurses were assigned to talk to, fondle and play with each. Acceleration of motor, adaptive and speech behaviour was apparent after two months. Goldfarb (1943, 1943a and 1944) described the effects of institutional life on the child as producing lack of differentiation of the personality, with deficient inhibition and control, and a passivity or apathy of the personality. He considered that such children were more fearful, less thoughtful, less ambitious, less capable of sustained effort, less capable of feeling guilt and less likely to make satisfactory personal and social relationships. From a study of 40 children who had been in foster-homes from early infancy, he concluded that institutional life predisposed them to failure in adjustment to foster care (*cf.* Goldfarb and Klopfer).

Some confirmation of these findings was given by Wright (1942) in children over 5 and by Muench (1944) in adult males in whom an increase in I.Q. was noted.

Neuer (1947) has summed up the nature versus nurture controversy in his

declaration that the *prevention* of mental deficiency is only possible by dealing with environmental factors. Mental traits in themselves are not inherited, but only the structures which enable the individual to react. For the development of the cognitive functions adequate environmental stimulation is necessary. He stresses the importance of the mother as a teacher from whom the child derives his first impressions, his interpretations, and his instinctual satisfaction. She, more than anyone else, is the child's cultural background from whom he derives his early sense of goodness, beauty and truth. Next in importance and in order are the father, the sibs and school and social group. The younger the child the more important the environmental influence. In his view familial or undifferentiated types are socially handicapped, victims of an unhealthy family atmosphere. "In these persons the chaotic conative and emotional trends have become less obvious than the intellectual deficit."

Lurie (1946) is also of the opinion that heredity is a minor factor in the etiology of feeble-mindedness.

Fried and Mayer (1948) have been able to demonstrate the importance of socio-emotional adjustment in the physical growth of dependent and neglected children brought up in a special institution. They found, in general, a close correlation between the rate of growth and the degree of emotional adjustment.

EDUCATIONAL ASPECTS.

The subject of special education for the defective is such an important one that it can hardly be dealt with adequately in such an article as this, but brief reference must be made to some of its many aspects. These include :

Habit training for idiots (Morales, 1942).

Training for low-grades in percussion bands, physical exercise, elementary sense training and occupations (Fitzgerald, 1946).

Pre-academic programmes for mental ages less than 8 (Patterson, 1947 ; Weiner, 1946, 1947).

Speech therapy (Cobb, 1943 ; Rose, 1943 ; Russell, 1947 ; Allen, 1947 ; Huber, 1942).

Special training for the deaf, deaf-mutes and the word deaf (Currier, 1946 ; Russell, 1943 ; Heider, 1948 ; Macfarlan, 1948 ; Wishart, 1947).

Special education for the blind (Maxfield, 1944 ; Langan, 1948).

Extensive attention to the education of the brain-injured (Lehtinen and Strauss, 1944 ; Strauss and Lehtinen, 1947 ; Collis, 1947).

Facilities for the slow learner (Rasmus, 1946 ; Rosebrook, 1945).

Consideration of the problems of general backwardness (Schonell, 1942 ; Graham, 1947 ; Millais, 1947).

Academic education for retarded children with I.Q's. 40-66 (Traill and Douglas, 1947).

Specific reference to problems of special backwardness, e.g. arithmetic (Cruickshank, 1948 ; Carrison and Werner, 1943) ; reading (Günzburg, 1948).

Musical training (Prather, 1947 ; Bowers, 1946).

Manual instruction (Landes, 1945).

Vocational and occupational training (Lovell, 1947 ; De Prospro, 1947).

Religious instruction (Burke, 1947 ; Schomer, 1946).

Programme for delinquents (Buchan, 1943).

For the diagnosis of specific backwardness, Schonell (1942) proposes the following scheme of inquiry :

1. Measurement of general intelligence.
2. Application of scholastic tests.
3. Application of diagnostic tests in backward subjects.
4. Application of sensory tests, e.g. for vision and hearing, and the use of the audiometer and gramophone.
5. Assessment of emotional characteristics e.g. self-confidence, persistence assertiveness, attention to detail, sensitiveness to approval, concentration, self-regarding sentiment, attitude to school work, and emotional stability.
6. Record of interests.
7. Inquiry into personal history.
8. Inquiry into educational history in backward subjects.
9. Talk *re* anxieties and conflicts, and use of play therapy.

The general principles of special education for the mentally retarded are discussed by Beaman (1943).

A number of observations have been made indicating differences in mental aptitudes between the " brain-injured " and " non-brain-injured " defectives. The brain-injured child's thought-processes are noteworthy for their unexpectedness. Associations are rather fluid, and appear to overrun the expected bounds of past, present and future. In contrast to the endogenous type of defective whose thought-processes concern objects, appear static, general, with some tendency towards abstractions, the brain-injured's thoughts appear more dynamic, over-dramatic, separating essential from non-essential detail with difficulty, rather fantastic, and lacking in control and discipline (Strauss, 1944 ; Werner and Strauss, 1943), though his vocabulary and word-definitions are more mature than those of other defectives (Bijou and Werner, 1944). When tested with the tachistoscope, the brain-injured child has difficulty in appreciating motion, and sees the individual " flashes " without relating them sequentially (Werner and Thuma, 1942). As compared with other defectives, he is more " animistic " and endows inanimate objects with feelings and spitefulness (Werner and Carrison, 1944). Some of these features can be brought out by Rorschach tests (Werner, 1945, and Hackbusch, 1947). Lehtinen and Strauss (1944 and 1947) have related these differences to their educational needs. Others have written on the study of defectives by the Rorschach technique (Hackbusch, 1947 ; Sloan, 1947 ; and Jolles, 1947).

Language disability may be due to injury, disease, or physical or mental abnormalities. Eustis (1947) proposes to use the term " specific language disabilities " for specific reading disability, speech defects, such as lisping and stuttering, and motor speech delay.

Specific reading disability is due to an uncertainty in spatial orientation, a confusion between the right-left, and the left-right directions, which lead to reversal of individual syllables—a kind of mirror speech. The disability is encouraged by " look and say " methods of teaching, and should be treated by

postponement of teaching for reading, and by the use of phonetic and kinaesthetic methods.

The author describes a family tree covering four generations to illustrate the familial nature of the condition, and suggests that the full syndrome includes left-handedness and ambidexterity, bodily clumsiness as well as speech and language disabilities. The fundamental nature of the condition is a process of slowing of maturation, dependent on slow tempo of myelination of motor and association nerve tracts. The condition is commoner in boys than in girls, in the ratio of 3 : 1.

In another paper (Eustis 1947a) the author discusses the relationship between the syndrome and problem behaviour which arose in 13 of 23 cases. Theta Wolf (1945) is of the opinion that the causes include ocular muscle imbalance, islands of deafness and too standardized methods of teaching. It is complicated by faulty attitudes on the part of teacher or parent. Left-handedness, mixed eye-hand dominance, and failure to establish dominance in cerebral hemispheres should be excluded (Aten, 1947).

BEHAVIOUR DISORDERS AND MENTAL DEFICIENCY.

Although it is usual to take as a general estimate the figure of 80-90 per cent. as representative of the relative incidence of primary oligophrenia among the general defective population, when we come to investigate the relative proportions of different factors operative in the behaviour disorders among defectives, the importance of environmental factors becomes apparent. Fairweather (1948) took three groups of patients: (a) 500 consecutive admissions of the general defective population at Stoke Park, (b) 62 male and 48 female defectives of Stoke Park certified under sections 8 and 9, and (c) a Rampton group of 52 illiterate males attending 3R classes, and assessed the relative incidence of the following factors for each group, as follows:

	Group (a).	Group (b).	Group (c).
Orphanism	28.6%	33.6%	52.3%
Illegitimacy	14.8%	17.3%	25%
Parental desertion	8.2%	14.5%	11.4%
Family history of psychosis	4.4%	5.5%	15.9%
Family history of mental defect	13.4%	35.5%	22.7%

Marcotte, (1947) in a more intensive study of behaviour difficulties in 20 defectives, concluded that mental deficiency by itself is not a sufficient explanation for lapses in conduct, and stressed that treatment should be directed to such relevant factors in order of importance, as parental rejection, usually on the part of the mother, unsatisfactory parental interrelationships, unsatisfactory sib to sib relationships, and inadequate teacher to pupil relationships. The important point was made that it is common to find multiple factors operative.

Neuer (1947) estimated the relative incidence of different types of behaviour disorders associated with mental deficiency in 200 patients as follows:

(1) Organ-pathology group of structural or physico-chemical nature, 39.3 per cent., made up of 65 per cent. of all idiots, 35 per cent. of all imbeciles, and 18 per cent. of all morons.

(2) (a) Neuro-psychotic group (minor or major psychoses), 28.3 per cent.

(b) Simple type—belonging to the subcultural group, 32.4 per cent.

He concludes that emotional disturbances, inferior cultural milieu and sub-standard economic conditions are mainly responsible for the problem presented by high-grade mental deficiency, and that mental deficiency in the neuro-psychotic group is the result and not the underlying cause of the minor or major psychosis.

Fairweather (1947) analysed the total number (262) of admissions of violent and dangerous juvenile defectives to Rampton into the following overlapping groups:

- | | | |
|-----|---|-------|
| (1) | Cases with a definite history of mental defect in sibs or parents without mention of environmental factors | 4.6% |
| (2) | „ of presumed hereditary influence | 13.0% |
| (3) | „ with a history of familial psychoses | 9.5% |
| (4) | „ with history of both familial mental defect and gross environmental factors | 16.8% |
| (5) | „ with gross environmental factors, e.g. orphanism, illegitimacy, parental dysharmony, poverty and slum conditions, or other evidence of social incompetence (e.g. prison record, alcoholism, etc.) without history of familial mental defect | 50% |
| (6) | „ complicated by physical disease, e.g. post-encephalitis, epilepsy, cerebral palsy, cerebral trauma, etc. | 84% |
| (7) | „ with insufficient history | 9.2% |

Paddle (1947) classifying the high-grade unstable defective according to instinctual deviations, found the commonest to be the sexual, pugnacious, acquisitive and self-assertive groups. He reaffirms the importance of such environmental factors as bad example and loose discipline and stresses the need for care in special institutions.

Schumacher (1946) contends that the behaviour difficulties in mental defectives spring from the child's reactions to the parents' aggression, resentment and hostility, when they become aware of his inability to progress normally. The child feels a greater sense of insecurity, which makes him more hostile and aggressive. Thus a vicious circle is produced in which effort and frustration lead to counter-aggression. Whatever capacity for growth and development the child may have had is misdirected and mis-spent, and the situation becomes aggravated by the lack of normal relations with other children. The psychoanalysts have rightly stressed the adverse effect of prolonged separations of mother and child in infancy and early childhood, on the child's capacity for making good personal relations in later life (Edelston, 1943; Freud, 1944; and Friedlander, 1948). Bowlby (1946) has specifically related persistent delinquency to such prolonged separations.

Smith (1947) is of the opinion that to treat criminal types with ordinary defectives is to prejudice the training of the latter. He draws attention to the use of the social maturity scale for differential diagnosis. Similarly, Bodman (1946) and Dunsdon (1947) have referred to the delinquent's social incompetence as measured by the social quotient. A comprehensive account of the subnormal adolescent girl has been given by Abel and Kinder (1942), and the problem was the subject of a special committee of magistrates and the B.M.A. (*Brit. med. J.*, 1946).

The relationship of mental deficiency to the psychoses has been investigated by Ravn (1947) and Pollock (1944 and 1945), while Rohan (1946) has reviewed the types of psychoses occurring in 39 defectives. The very important question of the psychoses of childhood in relation to mental deficiency calls for detailed inquiry that so far has not been forthcoming, though it has been touched upon by various writers (Bender, 1947; Yerbury and Newell, 1942; Bradley, 1947).

MENTAL DEFICIENCY AND THE SERVICES.

Although many of the problems connected with the selection of trainees for the services have lost some of their topical interest, some sociological interest is to be found in a study of the findings of different observers with regard to personnel selection and the general stability of the defective under war conditions.

The methods of selecting recruits for the Royal Navy were outlined by Rodger (1947), and Curran and Fraser Roberts (1945), and the screening methods employed for the American Navy were elaborated by a number of different writers (Wittson *et al.*, 1942; Wittson *et al.*, 1943; Hunt *et al.*, 1943; M. A. and C. Wright, 1943; Hunt and Older, 1944; Hunt *et al.*, 1944; see also *Am. J. Ment. Defic.*, 1942).

Vernon (1947) gave a detailed account of the methods used for the Royal Navy, the Army and the A.T.S., and stressed the point that tests were an aid to the personal interview, and not a substitute for it. The special methods for eliminating defectives from the Army were described by Menninger (1943).

Boshes (1942) quotes the British experience that all men with a mental age up to the 8-year level, 86 per cent. between levels 8-9 years, 33 per cent. with mental ages of 10, and 28 per cent. with mental ages of 11 are untrainable.

Wittson *et al.* (1942a), defined the incidence of different kinds of neuro-psychiatric unfitness in 600 unselected cases as follows: mental deficiency 33 per cent.; constitutional psychopathic state and inferiority, 26 per cent.; neurological disorders, 24 per cent.; psychoneuroses, 8 per cent.; psychoses, 5 per cent.; and illiteracy, 4 per cent.

Karpinos (1946) classified the main reasons for rejection of 33.49 per cent. of recruits for the American Army and Navy as 14.10 per cent. for psychological reasons, i.e. 5.5 per cent. for defective intelligence, 8.6 per cent. for psychiatric disorders; 17.76 per cent. for physical defects; and 1.63 per cent. for administrative reasons, of whom some were illiterates.

Rowntree *et al.* (1943) gave the causes for rejection in 42,273 whites and 3,312 negroes, forming 237 and 455 per thousand respectively. While educational deficiency was the eighth in order of importance among the whites,

it was first in order among the negroes, in whom, with syphilis, it accounted for half the total number of rejects. Mental deficiency was placed in the tenth place in order of importance among the whites, and ninth among the negroes.

Frankel (1944) compared the rejection rates for educational and mental defectives. For all ages, the number of rejects for educational defectiveness was 55.2 per thousand, and for mental deficiency 11.8. For those of 18 and 19 years the figures were 19.5 and 7.0 per thousand respectively.

The wide variation in the figures given by different observers is indicated by Wittson *et al.* (1943), who placed psychopathic personality and mental deficiency as the leading causes for discharge, with epilepsy and the organic disorders coming third.

Hyde and Kingsley (1944), in a survey of the rejection rates at the Boston induction station, gave some indication of the reasons for these differences in their comparison of the population densities of the communities from which selectees came. Thus they noted that the highest rates of incidence for mental deficiency occurred in those from semi-rural areas, and the lowest rates were found in those from small cities. This was, to some extent, irrespective of factors of socio-economic level and national origin.

Sims (1946), however, noted considerable variation in the incidence of mental deficiency among different national groups admitted to a psychiatric base hospital.

Weaver (1946) surveyed 8,000 army defectives to determine how they would adjust to army life, and what factors operated to aid or hinder their adjustment; 44 per cent. of the men and 38 per cent. of the women were maladjusted enough to necessitate their discharge. Their maladjustments were due to ineffectiveness, psychopathy, antisocial behaviour and psychiatric and psychosomatic reactions. The mean I.Q. was 68. There was no appreciable relationship between successful adjustment and the level of maturity measured by the Wechsler-Bellevue Scale and the Kent and Army specialist classification tests. The mean I.Q. of the remainder was 72, and the author concluded that since more than half of the defective group adjusted satisfactorily to the rigours of army life, a revaluation of the defectives' service to the community was indicated. Similar views are expressed by Butler (1945) and Coakley (1945).

Doll (1943) expressed the opinion that while some endogenous high-grade morons attained a degree of success in the services, this was hardly sufficient to warrant the hazard and cost of the nine others like him who were military liabilities. Of the exogenous cases, very few were able to stand the stress of war when this became more acute.

Ballard and Miller (1944) estimated that of 2,000 successive patients admitted to an R.A.F. centre, 3 per cent. were mental defectives who were referred for hysterical symptoms, ineffectiveness, or for minor disciplinary offences. Dewan (1948), in a report on the clinical findings in the examination of over 30,000 Canadian recruits, concluded that there was a very definite correlation between emotional stability and intelligence. The rate of incidence of psychoneurosis and other patterns of emotional stability declined as the degree of intelligence advanced, although 12 per cent. of the men of very superior

intelligence had to be rejected because of emotional instability. The writer expresses the opinion that the instability of the defective is a reflection of the instability of the early environment, due in turn to poor parental stock.

THE PREVENTION OF MENTAL DEFICIENCY.

Benda (1942) considers that little can be done in the way of the prevention of feeble-mindedness because in relation to the total population the number of feeble-minded persons is a biological proportion which cannot be changed. There are, however, a number of pathological factors capable of modification which can be best appreciated by classifying the causes of idiocy and imbecility (exclusive of mongolism) as follows :

Classification.	Ante-natal.	Natal.	Post-natal.
Idiots	50·3%	31·3%	18·4%
Imbeciles	40%	9·1%	50·9%

Apart from attention to the abuse of abortifacients, alcohol and drugs, he considers that little can be done by way of prevention of the developmental failures in the prenatal period. More than 31 per cent of all cases of idiocy, however, and 9 per cent. of all cases of imbecility are caused by birth injuries or natal factors. These include all accidental, vascular and anoxaemic factors connected with birth. Prophylaxis by way of special care of the premature child, by the use of vitamin K, incubators, and improved methods of feeding (*cf.* Levine and Gordon, 1942) should lead to a considerable reduction of these figures.

Benda and Tadgell (1942) estimate that syphilis is present in 5 to 6 per cent. of the feeble-minded population, but that it does not cause mental deficiency as often as this percentage indicates, since many feeble-minded congenital syphilitics are so because of hereditary factors, and would be so even without syphilis. Ramsay (1942), however, suggests that the estimate should be placed higher because congenital syphilis does not always show a reaction to the blood test, but may none the less be the cause of injury to the germ-plasm of the parents.

As far as mongolism is concerned, Benda *et al.* (1943) consider that early diagnosis may be made in pregnancy, with the possibility of adequate substitution therapy when more is known about the exact endocrine deficiency present.

Neuer (1947) considers that the role of preventive psychiatry in mental deficiency involves two quite distinct spheres: (*a*) Disorders correlated with organ pathology, concerning especially gynaecologists, obstetricians, pediatricians and public health officers; and (*b*) disorders not correlated with organ pathology, but concerned with the general improvement of education and economic conditions. The principles of treatment relating to mental deficiency should include, therefore, provision of special hospitals for those with organ pathology, family homes containing not more than ten children to each unit, for socially handicapped children, colonies for socially handicapped

adolescents, colonies for socially handicapped adults, and special institutions for delinquents.

He emphasizes the need for a different approach to each special group and strongly suggests that at present there is great danger of making segregation an additional cause of mental retardation.

LEGISLATION RELATING TO MENTAL DEFICIENCY.

A memorandum issued by the Council of the British Medical Association (*Brit. med. J.*, 1947), clarifies the interpretation of the definitions of the Mental Deficiency Act, 1927. It is pointed out that the concept of mind is wider than that of intellect, and that mental defect is not the same thing as intellectual deficiency, though it includes it. Unsoundness of mind is now defined as "an impaired condition of the mental functions involving the intellect, emotions and will, or one or more of these functions, which are in fact only divisible for purposes of classification."

The memorandum suggests that the term "moral defective" could be discarded. It also indicates that mental deficiency may not be permanent, and that attention to environmental factors may lead to amelioration, whereas the previous emphasis on innate and hereditary factors implied that improvement was most unlikely.

The importance of social adaptation or social efficiency is stressed, and the point is made that mental deficiency may be present even in the absence of scholastic backwardness.

The change of emphasis is further shown in the addendum on psychopathic personalities and it is suggested that many of these would be dealt with adequately under the Mental Deficiency Acts.

The Education Act, 1944, provides for new legal categories, among which are the educationally subnormal and maladjusted (Regulations, 1945). Special facilities for training are now offered to children in these categories. No child who is capable of education within the school system is called a mental defective, and this change is reflected in the new definition of feeble-minded persons, "that is to say, persons in whose case there exists mental defectiveness which, though not amounting to imbecility, is yet so pronounced that they require care, supervision and control, for their own protection or for the protection of others, or, in the case of children, involves disability of mind of such a nature and extent as to make them, for the purposes of section 57 of the Education Act, 1944, incapable of receiving education at school." The Act allows the parent to appeal to the Minister of Education against the decision for special educational treatment, or for reference to the local mental deficiency authority.

If a child comes before the Court the action taken will depend on whether he is considered able to remain within the school system. If he is so considered he may be committed to the care of the local education authority, as a "fit person," or be committed to an approved school. If he is not so considered the Court may direct that a petition be presented, or may itself direct the child to a mental deficiency institution.

Other changes brought about by the National Health Service Act, 1946, and the Disabled Persons (Employment) Act, 1944, in so far as they relate to mental deficiency, are referred to in a pamphlet issued by the National Association for Mental Health (1948).

(See also Mental Deficiency Regulations, 1948.)

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DELINQUENCY AND CRIME.

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INTRODUCTION.

THE present situation regarding delinquency and crime is a serious menace to social health, not only because the number of offenders is increasing, but also because serious crimes are more frequent. The prison population in the years just before World War II was less than 11,000. In 1947 it reached 17,101 and was still rising. In their Report for 1947 the Prison Commissioners point out that this reversion to conditions which have not been seen for some 40 years is the more disturbing as the peak has clearly not yet been reached. Compared with the year 1938, the receptions into prison for sexual offences committed by males increased by nearly one-third; for crimes of violence, including murder, manslaughter and wounding, by more than one-third; for burglary, housebreaking and receiving, the figure was more than doubled; and the number of cases of bigamy was quadrupled. There were also substantial increases in crimes committed by women and girls.

In the year 1947 there were 371 offenders received into prison who were insane, and 327 were mentally defective. The average for the preceding five years was 373 insane and 373 mentally defective. In 1938 the figures were 465 and 273 respectively. It is reasonable to believe that the difficulties and frustrations of life to-day are not reflected among the insane and mentally defective potential offenders to the same extent as they are among the general population of potential law-breakers. The proportion of subnormals, psychoneurotic and psychopathic personalities in the general prison population is unassessed, and their relative position undetermined.

JUVENILE DELINQUENCY.

The term delinquency refers here to both minor and major offences in young persons of either sex. The proportion of offenders per 100,000 of the population in each age group is highest in the groups 8-14 years, and 14-17. Thereafter there is a continuous diminution in each age group.

A "child" is defined in law as a person under the age of 14, and a "young person" as one who has attained the age of 14 and is under the age of 17. No child under the age of 8, in this country, can be guilty of any offence. A young person cannot be ordered to be imprisoned for any offence unless the court certifies that he is of so unruly a character that he cannot be detained in a remand home, or that he is of so depraved a character that he is not a fit person to be so detained.

Magistrates' courts deal with juveniles found guilty of indictable offences by probation, by dismissal or binding over without supervision, by a period of detention in an Approved School, or by a fine.

The Criminal Justice Bill, 1947, prohibits a court of summary jurisdiction from imposing imprisonment on a person under 17 years of age, and a court of assize or quarter sessions from imposing imprisonment on a person under 15 years of age. The Bill also prohibits a court from imposing imprisonment on a person under 21 years of age, unless the court is of opinion that no other method of dealing with him is appropriate. Further, when a court has power to impose imprisonment on a person who appears to the court to be not less than 14 but under 21 years of age, the court may, if it has been notified by the Secretary of State that a *detention centre* is available for the reception from the court of persons of his own class and description, order him to be detained in a detention centre, to be specified in the order, for a term of three months. In certain circumstances the detention may be for any term not exceeding six months, or the maximum term of imprisonment, whichever is the shorter.

The Home Secretary may provide *remand centres* for the detention of young offenders who are remanded, or committed in custody, for the purpose of obtaining a medical report on their physical or mental condition, for the assistance of the court in determining the most suitable method of dealing with their cases, and facilities for observation are to be provided.*

These legal changes should go far to select the young offender who requires medical treatment, and to provide him with assistance when he is most in need of expert medical advice. It is common knowledge that it is difficult to exaggerate the importance of the group of offenders under consideration, since many recidivist careers begin at this period of life. In recent years much thought and many investigations have been carried out in an attempt to deal with the problems involved. In this quest lawyers, doctors, social workers and others have taken part in assisting the executive authorities.

Kennedy (1947) points out that if the juvenile court magistrate is to do justice to-day to the children who come before him, he must bring to his aid some of the method of science, *i.e.* the method of patient gathering of facts, comparing them with previous facts, taking action only after careful consideration, observing results and applying them to future cases. He refers to the fact that the psychiatrist makes use of the investigations of a team of workers, and assesses the relevance of the work of each in relation to the child's attitude of mind and the mental dynamics of his behaviour, in order to present to the court, concisely and in plain language, the potentialities and deficiencies of the child's mental state, his personal and social difficulties, and the probable reason for his delinquent behaviour. At the same time, Kennedy warns the

* For the sake of continuity it may be added that, in addition to the above, the Criminal Justice Act, 1948, with certain provisos, enacts that where a court of summary jurisdiction has power to impose imprisonment on a person who is not less than 12 but under 21 years of age, or to deal with any such person under Section 6 of the Act for failure to comply with any of the requirements of a probation order, the court may, if it has been notified by the Secretary of State that an *attendance centre* is available for the reception from the court of persons of his class or description, order him to attend at such a centre to be specified in the order for such number of hours, not exceeding twelve in the aggregate, as may be specified. Provisions prevent the order being made if the person has been previously sentenced to imprisonment, Borstal training, or detention in a detention centre, or has been ordered to be sent to an Approved School. He shall attend, so far as is possible, at times which will not interfere with his school or working hours, and for not more than one occasion on any day, or for more than three hours on any occasion.

psychiatrist in this field against over-confidence. He advances the moderate view that a psychiatrist cannot know enough about the background of delinquency until he has spent at least a year or so in examining cases, and has had some contact with each of the many agencies concerned with child welfare. He also insists that theoretical training in psychiatry needs very great modification when it is applied to this highly practical subject. Moodie (1946) contends that psychiatric theory applied to delinquency has, in its application, hindered progress by creating the belief that the whole matter is so deep and delicate that no direct methods to deal with it should even be tried. He reminds us that this belief has given free rein to those who consider that crime is a mental disorder, and has inhibited common sense in their efforts to relieve it. Dicks (1947) cautions the over-enthusiastic more generally, and states that psychopathology and psychotherapy will probably never become exact sciences in the mathematical sense. To expect exactitude during a time when concepts are still developing is premature.

The whole body of citizens is directly or indirectly concerned with delinquency and crime. Ignorance and confusion of thought regarding the essentials of crime and punishment is common among laymen. The theorists who declare that there would be no neurosis if a maximum gratification of instinctual urges was allowed, have done much harm. Moodie (1947) refers to the misconception that no emotions must be suppressed if the mental health and balance are to be maintained. He points out that the term repression is used in psycho-analysis to indicate an entirely theoretical process by which the mind keeps unacceptable thoughts out of the stream of conscious thinking. It has nothing to do with ordinary thoughts or behaviour, and in no way contraindicates the use of self-control or discipline in ordinary life. He adds that repression is healthy and normal; faulty repression is harmful and unhealthy, and may lead to mental distortion and even insanity. As Moodie was here writing for ordinary doctors, it may be hoped that through them his views may reach many parents who are perplexed as to the wise method of training their children in social behaviour. In this, as in other matters concerning delinquency and crime, a monopolist approach is often misleading. Few will believe that it is beyond the wisdom of the ordinary parent to exercise necessary control, while helping the child to express his feelings in a manner which relieves him without injuring himself or others.

Writing for the medical reader, regardless of the particular stage in his career, Clark-Kennedy (1947) stresses the fact that where there are no moral standards, or the social conventions are not accepted as a basis for determining behaviour, there can be resentment and a feeling of frustration but no moral conflict. Can we doubt that by educating the child to give full expression to his out-fanned desires, regardless of the effect of such abandon on others, we produce emotional difficulties which must be faced sooner or later, and are less hard to bear during pupillage?

An anonymous writer (1947) calls attention to the fact that science cannot be expected to solve easily the secrets of the physical and psychological structure of man. He believes that certain Utopians have done ill by pretending to resolve, by premature psychological interpretation and hasty psychiatric

diagnoses, controversial questions when both sciences are still in their primary stages of development. At least this may be said, both sciences are in the early stages of applying their knowledge to the practical problems of criminality. It is relevant to add that many observers believe that the science of government is also in a primary stage of development. To the onlooker it seems to proceed haltingly by the method of trial and error, and at the same time frequently to disregard the lessons to be learnt from past, and even current, history. Perhaps Margery Fry (1947) had something of this in mind when considering the general movement of laws relating to young offenders. She believes that in every country there is now a wealth of experience in the actual handling of juvenile offenders, and of the social, medical and psychological causes of their conduct, but at the same time there is an acute sense of the paucity of remedial methods, which calls for new forms of treatment.

Statements are sometimes made by psychologists on psychiatric matters which are misleading, and some medical psychotherapists seem to attach small importance to psychiatric diagnosis. In forensic situations lengthy digressions on the theory and practice of psychotherapy divert attention from the essentials of the case, which can be presented explicitly after a psychiatric diagnosis is made. Moreover, in delinquent cases only a psychiatric opinion can authoritatively exclude declared or incipient mental disorder.

Magistrates in a juvenile court have no authority to order an examination of a child merely to provide evidence for the prosecution. Having decided that a child is guilty or is in need of care or protection, they have power to order a medical examination, whether the child or his parents agree or not. Difficulty may arise if the report introduces criticism of the parents' conduct. The rules allow reports to be put in without being shown to the child or his parents. T. H. Giles (1946) points out that this does not mean that undisclosed reports are to be the rule and not the exception. Material criticism of the conduct of the child or his parents must be told them, but the rule does not require the magistrate to disclose the source of the information, unless its accuracy is challenged and it is thought necessary to establish its truth by calling evidence. The importance of the matter is apparent when it is remembered that, as a result of his experience as Chief Clerk to the London Juvenile Courts, Giles found from the psychological reports submitted to the courts how much delinquency is due to incompetent and unwise parents, and how greatly problem parents exceed problem children. Carr-Saunders, Mannheim and Rhodes (1942), Miller (1944), Pearce (1944), Moodie (1947), Roper (1947) and others emphasize the importance of the parent-child relationship in connection with juvenile delinquency. Leavitt (1947), Wooley (1947), Goitein (1947), Bender (1947) and others in America refer to its significance, and Leavitt notes the fact that the history of delinquents in the United States of America shows a high percentage of parental difficulties, divorce, separation, broken homes, dependency, neuroticism and psychoses. East (1942) points out that the evasion of parental duty is often more reprehensible and more in need of study and correction than the consequent legal misconduct of the child. He suggests that liaison between the parent and school-teacher is not always sufficiently exploited.

Banaister and Ravden (1944) analysed some of the data regarding 112 children who were referred to the Cambridge Child Guidance Clinic. They found nervous symptoms were largely correlated with accord homes, and delinquency with broken homes. There was some evidence which suggested that the child who is referred to the clinic from the accord home is liable to have been over-protected, and that lack of affection is connected with the same symptoms. Inadequate or improper discipline was found in over 66 per cent. of the cases, and is connected with nervousness in the accord home and with delinquency in the broken home. In a later paper (1945) these observers consider a control group of 93 children who had not been referred to the clinic and were apparently well adjusted. They concluded that it is not a chance factor that many problem children come from broken homes, and they believe that this association may, to a considerable extent, be due to the psychological effects of instability in the parents. Since some satisfactorily adjusted children come from broken homes of various kinds, the suggestion is made that satisfactory adjustment depends largely on the provision of a close psychological substitute for a normal home. There was no reason to suppose that an only child is handicapped as a consequence in either group. The writers found that well-adjusted children have much more strongly developed interests and hobbies, as well as social activities, than the problem children. In particular there was much less frequent attendances at cinemas.

Otterström (1946) reported, as the result of a large-scale enquiry undertaken by the State Institution of Human Genetics in Sweden, that children coming from homes in which the parents were drunkards or criminals were especially liable to commit crime or need public assistance when grown up. No significant differences were found on comparing the after-histories of illegitimate children, or children from broken homes with those of legitimate children or those coming from normal homes.

Sadler (1947) believes that society is dealing with juvenile crime ineffectively. Home influence and religious authority are loosening and young people grow up viewing a panorama of broken and loveless homes, orphan asylums, juvenile courts and prisons, all vivid testimony to society's failures. With this confusion and wastage it is not strange that restless and adventurous youths endeavour to solve their own difficulties, and in so doing often become delinquent. Judge Earengy (1947) refers to the matter as seen from the purview of a county court. He calls attention to the fact that there can be no real privacy or separate family life in the tenement houses of to-day, and in consequence parental influence decreases to the vanishing point. He is convinced that much of the baseness of behaviour tending to immorality and crime in, but by no means confined to, the classes brought up in tenements is substantially due to the bad housing conditions, but Mannheim (1947), in an interesting study, finds that some of the new housing estates in the Cambridge area show a considerably higher incidence of juvenile delinquency than the town as a whole. He considers that housing in itself is no panacea for social evils, unless accompanied by social services such as youth centres and other measures which deal with some of the needs of a youthful community. The

significance of these findings is emphasized by the fact that, unlike adult crime, juvenile crime is usually an expression of group activity.

Reference is due to the part which is carried out by the Police in this country in the prevention of juvenile crime. Sir Harold Scott (1947) refers to the fact that throughout the Metropolitan Police area, police officers continue to devote much of their own time to the Youth Club Movement, and that there is good reason to believe that the healthy influence of these clubs is reflected in the marked drop in juvenile crime in those areas in which they are situated.

A study of the literature and practical experience leaves one in no doubt that further investigations into the causes, prevention and treatment of juvenile delinquency are urgently required. The Governor of a Borstal Institution (1946) states that the upbringing of the inmates, and their domestic surroundings, companions, and mode of life seem to have produced an entirely selfish philosophy. Another Borstal Governor considers that the generation of lads entering these institutions has but the faintest conception of what is meant by honesty, truth, and uprightness. Honesty is regarded as outmoded, truth is a virtue only when it cannot be denied, and uprightness a form of stupidity preached by those who clearly suffer from a narrow-minded conception of life. Opinions such as these, founded upon a longitudinal section of the boys' lives, show how extensive is the problem of juvenile delinquency. At the same time, amid so much that is obscure and sometimes apparently contradictory, the fact that many delinquents come from good homes, and many non-delinquents from bad homes, stresses the importance of the personality factor as a cause of delinquent and non-delinquent behaviour.

Gillespie (1944) doubts whether it is logically necessary to insist on the parallel presence of psychoneurotic symptoms, in the ordinary sense, in coming to the conclusion that the criminal act is to be regarded as a psychoneurotic symptom. He considers that the criminal act as the expression of a conflict exactly homologous with the kind of a conflict that would produce in others a psychoneurotic symptom, is much commoner than the association of psychoneurotic syndromes and criminal acts. Here, also, the observation seems to stress the significance of personality.

CRIME IN ADOLESCENCE.

As the lad passes from juvenility to adolescence he is faced, and sometimes abruptly, not only with an ever-widening horizon but with an unfolding view of a modern world which is frequently ugly and sometimes evil. Yet he is expected to attain a degree of social maturity although he is obstructed in his efforts by many adverse influences. Those who sit in judgment may relieve themselves of some conceit if they remember that the older generation was largely responsible for our present discontents, and that for this reason many adolescents fail to reach social maturity by the direct route. Perhaps one of the neglected factors in the prevention of adolescent crime to-day is the avoidance of fatigue, discontent and lack of interest at work. Vocational guidance and selection by industrial psychologists have been perhaps insuffi-

ciently exploited. The difficult problem of leisure, too, is not always sufficiently turned to good account.

Among the improvements in the treatment of adolescent offenders may be noted the steady development of vocational training in Borstal institutions, the educational facilities which have enabled a number of the lads to become engaged in correspondence courses provided by the British Institute of Engineering Technology, the opportunities to study for the matriculation examination of London University, and the fact that selected lads in certain Borstal institutions have been admitted to classes in technical colleges.

CRIME IN MATURITY AND SENESCENCE.

Crime in maturity has been discussed by East (1946). He finds that the figures for the ten-year period, 1929-38, show that when persons of both sexes convicted at assizes and quarter sessions, together with those convicted of indictable offences at courts of summary jurisdiction, are considered in age and offence groups, a variation in frequency occurs. Between the ages of 21 to 50 the order of frequency is acquisitive, aggressive, sexual. Under the age of 21, and over the age of 50, the order is acquisitive, sexual, aggressive. There are no outstanding anomalies when particular offences are considered. Bigamy, for example, occupies, as might be expected, the first place among indictable sexual offences in the age group 30-50. Indecent assaults on women and girls are two and a half times more frequent in the age group up to 30 years than in the age group 30-50, and three times more frequent than in the age group over 50 years of age. The official figures show that, of the prisoners who were received into prison during the year 1930 without previous proved offences prior to first reception, the percentage of those who were not again received into prison, as far as was known, before the end of the year 1938 was highest over the age of 30. The figures suggest that in spite of the sobering effects of maturity a considerable proportion of first offenders reach middle age before they commit crime, but that a sentence of imprisonment is likely to have a deterrent effect upon the majority of them. It is perhaps at this age that the individual criminal is nearest to his normal self. He has sloughed off the disabilities of adolescence and is not yet encumbered by the incapacities of senescence. If a mature man commits crime, his return to normal social life will chiefly depend upon his own efforts, as he is generally less suggestible to the influence of reformers than the adolescent. Nonetheless, there is reason to think that with some of the older offenders insufficient use is made of the probation officer. East also refers to the fact that resilience is usually less in the later periods of middle age and becomes still less as age advances. He suggests that this fact influences the man who is convicted of a crime late in life. He is then more likely to experience alarm at the discrepancy between the crime and his ambitions, and is more willing to see the potentialities which had previously enabled him to live respectably. In a previous paper East (1944) stresses the importance to the senescent of his restricted environment and constantly narrowing circle of friends, and to the fact that the atmosphere surrounding him should be considered when assessing the appropriate award or method of treatment if he breaks

the law. Mannheim (1946) considers that criminal law has not yet become aware of the fact that we are living, not in an individualistic, but in a mass age, where everything has to be adapted to the use of mass methods. If this statement is accepted at its face value it seems that instead of dealing with the punishment and treatment of offenders on individualistic lines, as far as is just and practicable, we should send all prisoners to a detention establishment without discriminating between their different physical, mental, moral, and psychological states. If the passage and its implications are to be thus understood, the humanizing efforts of lawyers, the executive, prison administrators, doctors and others will be discarded, and mass punitive measures take their place, with adverse results.

The Gluecks (1945) conclude that the tendency to become less aggressive in antisocial behaviour is not attributable to the arrival of any particular chronological age period, but that something occurs with the passage of time in addition to mere ageing of the offenders that accounts for the improvement. It was not achievement of any particular age, but rather the achievement of adequate maturation, regardless of chronological age at which it occurred that was the significant factor. They believe that the possible value of predictive devices to judges in sentencing criminals cannot be over-emphasized. They point out that the so-called individualization of punishment is for the most part intuitive. They think that prognostic tables, based upon the actual results of treatment in hundreds of cases, would induce judges to individualize in terms of objective experience. Notwithstanding the attractiveness of new suggestions, the value of intuition, based on wide experience, will not be denied by medical men who see its importance in their daily work. Further, to rely upon prognostic tables in awarding sentences would seem to prevent justifiable risks being taken in favour of the accused, and to measure the changing potentialities of his life by the dead cyphers of the statistician.

THE EFFECT OF IMPRISONMENT ON MENTAL HEALTH.

Mallinson and Warren (1945), Pether (1945) and others have considered the effect of imprisonment on Service Prisoners of War. Bettelheim (1943), Bondy (1943) and others have written on the effect of detention in concentration and internment camps on the civilian population. Gibbens (1947) had special opportunities as a prisoner of war to observe cases of neurosis and psychosis occurring in a population of 25,000 prisoners, and later was in charge of cases of neurosis in repatriated prisoners. He also surveyed the writings of ex-prisoners of war and concentration camp prisoners. There was no evidence that imprisonment increased the incidence of psychiatric illness of clinical severity. The so-called "barbed-wire syndrome" was essentially physiological. He differentiates four stages of mental ill-health. First, a period of depression lasting for two or three months. Second, a period lasting a year or more, in which the majority of prisoners feel a constructive desire for some kind of personal and moral regeneration. Third, a period of crisis which varied in length and in which ill-discipline, escapes, and changes of work, or a temporary mental or physical illness, were noted. Fourth, the personality

changes called "barbed-wire disease" were unmistakably present and indicated that difficulties on release would follow. The chief features at this stage were a subjective difficulty in concentration and in consequence poor memory, an increasing tendency to ruminate whilst the imagination became more and more divorced from reality. The subject became easily fatigued mentally, and found it difficult to feel pleasure in anything. Objectively he was apathetic and irritable. He lacked persistence, and paranoid attitudes appeared. He did not seem depressed, and Gibbens suggests that his true personality appeared rather than a prison artefact. He agrees with Vischer (1919), that this change occurs however good the conditions may be, and he attaches less importance to the indeterminate nature of the sentence on prisoners of war than some other observers. He is impressed by the uncertainty which is one of the characteristics of free life. Experience in our civil prisons, however, shows how burdensome uncertainty regarding the repossession of freedom may be. The chief release symptoms noted by Gibbens were anxiety, depression, restlessness, lack of concentration, a desire to be alone, insomnia, excessive shyness with women, and a feeling that the home morals had deteriorated. Irritability and somatic anxiety were also noted. The most important feature was the disturbance of behaviour, and the final evidence of the breakdown was usually a complete intolerance of authority. Gibbens agrees with other observers who liken the symptoms to the experimental neurosis.

Kirman (1946) also found a remarkably small number of psychoses occurring in repatriated prisoners of war and internees in the Far East. The incidence of neurosis was negligible. The greatest number of cases became ill after release from captivity.

In the notorious Belsen concentration camp Niremberski (1946) found that the patients showed a complete absence of personal and moral ethics in the sheer struggle for existence. Fear, he states, was the cause of the reaction features observed. Dulling to a complete failure of social adaptation appeared, gregariousness was lost, and family ties had no meaning. The sense of values depreciated, memory was impaired, symptoms of terror or fear were general. Aggression and apathy were more marked in men than women. The population was, however, grossly undernourished, and when the British troops entered, of approximately 50,000 to 60,000 people, 10,000 were lying dead in the huts or about the camp.

The effect of ordinary civil imprisonment depends partly upon the national character traits of those detained, and partly upon the aims of the prison administration and the manner in which they are implemented. The British character, independent, respectful of authority only so long as it merits respect, freedom loving, courageous, generous, tolerant, and with a saving sense of humour, must be taken into account when assessing the effect of imprisonment upon the mental health of the civilian prisoners at home. Radzinowicz (1945) states that the English Prison System not only yields nothing in comparison with those of many other states, but even, in many respects, surpasses them. The prison administration has had the great merit of having acknowledged officially the need for an extensive reorganization of the system in force, and has boldly and clearly laid down the principles to be followed.

Roper (1947), with long experience as medical officer in English prisons, points out that the effect of imprisonment on any particular person is the product of many factors, of which the most important are his physical health, the length and nature of the sentence, the external events which are important to him, the manner in which he is controlled and the attitude which he displays towards his conviction and sentence. All prison medical officers will agree that the effect of imprisonment on physical health is good; the mortality rate is also exceptionally low. Roper finds that many psychosomatic illnesses disappear as the result of prison medical treatment and that this is more frequent than it was 20 years ago. It reflects the increased flexibility of modern prison administration. The prison sentence naturally divides itself into a beginning, a middle and an end. Roper finds that in the beginning and in the end the prisoner's mind is preoccupied with external events, past and future. In both periods the past and future can be advantageously discussed with the man, but neither period is good for training because his mind is divorced from intra-mural interests. It follows that a short sentence which has no middle is useless for training purposes, and is regarded with disfavour by the prison authorities for this reason. In the middle period repining is ended and release too remote to claim much attention. Although this period appears static to the man it is then that he can consolidate the lessons he has learnt. It is the most productive period for training. Long sentences may induce disinterest in work and monotony in the manner of life. Transfer from one prison to another, concerts, lectures, the wireless, a good library, and other modern administrative measures avoid the staleness which was formerly apparent in some cases. The most favourable results will be those in which reformation is a subjective experience. According to Roper, the most important factor in deciding the result of imprisonment is the man's attitude towards conviction and sentence. If regret for the offence is spontaneous or can be introduced, the outlook is favourable, both as regards contentment during confinement and social behaviour on release. The aim should be the attainment of a sense of guilt—that is, a realization of the injury done to himself as well as to society—without setting up defence reactions. Among other conclusions Roper considers that short or indeterminate sentences produce unsettlement, and long sentences produce no deleterious effect if properly managed.

A prison system must deal with normal men and women in unusual surroundings, and with abnormal persons, many of whom have consistently failed to establish themselves happily in a favourable environment. Others suffer from minor mental abnormalities or from personal and odd deviations of character. Taking the prison population as a whole, a minority reject the justice of their conviction and sentence, and tend to set up defence reactions. A small group of constitutional psychic inferiors generally require a leaning post to support them. Another small group of psychopathic personalities and a few psychoneurotics require special consideration in prison. The habitual criminal shows marked polar antithesis, and accepts imprisonment as the occasional and inevitable offset to his gambling successes. Personal experience shows that these groups supply most of the failures of the modern prison system. It may be noted that studies of the effect of imprisonment on the

mental health of the prisoners stresses the fact that the majority of them are not substantially different from law-abiding citizens.

It has been alleged that mental deterioration is inevitable if a man is imprisoned for more than ten years. When applied to this country the statement is not only misleading but is also unsupported by any scientific data. The fact that four-fifths of first offenders convicted of a "finger-printable offence" do not return to prison is some evidence that they, at least, have not suffered mentally from imprisonment, if social adjustment is the criterion. The fact that homicides in this country who have escaped the death penalty, and serve long years of imprisonment rarely commit further crimes on release is a clear indication that their social adjustment has not been adversely affected by prolonged detention. Of course, imprisonment inevitably affects some persons differently from others. The introvert attempts to solve his difficulties in one way, the extravert in another. The paranoid is a misfit in any surroundings. There is no reason to believe that psychiatric illness is caused by imprisonment *per se*. Also, there can be no doubt that the so-called prison psychoses are less frequent than formerly, and only appear in persons already predisposed to psychopathic or psychoneurotic reactions.

CRIMINAL RESPONSIBILITY.

In discussions on criminal responsibility it is still often forgotten that the criminal law is not concerned with morality as such, and does not use the word "wrong" in the dictionary sense. It insists that a wrong act means an act that is contrary to, and punishable by law. The onlookers, as well as those immediately concerned in a criminal trial, must still agree with Overholser (1939), that too many psychiatrists have been prone to look upon themselves as advocates rather than advisers of the courts. Moreover, evidence based upon the assumption that all anomalous behaviour is due to mental disease often, in a criminal court, travels in a circle. The jury are told that the behaviour of the accused was abnormal and that he is insane. During the cross-examination they are told that he is insane because his conduct is abnormal. It cannot be any surprise that evidence on these lines receives unfavourable comment from those who have to listen, and that juries so often refuse to accept it. For the gaps which occur in the reasoning of the witness, tend to become filled up with assumptions which are opposed to well-ascertained facts related to the crime, and do not require psychiatric knowledge to assess them. Sir Roland Burrows (1945) has contrasted the lawyer's ability to appreciate the nature and bearing of evidence with the lack of appreciation of some medical men of the significance of the facts and the bearing of the evidence. The former were trained to develop this ability, the latter were not. Indeed, a busy doctor must frequently make his judgments immediately and act upon them. He often has not time or opportunity to reach his decisions by the method of science.

Two matters require passing notice. First, the disputants sometimes forget that, in answer to the Lords' Questions II and III, following the case of McNaghten, the Judges added that the instructions regarding responsibility should be "accompanied with such observations and corrections as the circum-

stances of each particular case may require." In practice, if a judge is satisfied that the accused was insane at the time of the crime, he uses his discretion when addressing the jury, so that in this matter the law is elastic. Second, the verdict of the jury in a criminal trial that the accused is unfit to plead (insane on arraignment) does not involve the issue of criminal responsibility, as the defendant is not tried, although he may be if he recovers his sanity. This is common knowledge, but reference is made to it because it is still occasionally suggested that every insane person is unfit to plead—that is to say, is, through mental disease, unable to understand the nature of the charge, to challenge a juror,* to know the difference between a plea of guilty and not guilty, to follow the evidence or instruct his legal advisers. A moment's thought can hardly fail to expose to the psychiatrist the fallacy of the suggestion. But there is more. If accepted, the proposal would sometimes send, untried, an accused person capable of being tried, to detention during His Majesty's Pleasure, although he might be well able to set up a substantial defence, both as to his sanity and innocence.

It is also general knowledge that persons who are undoubtedly guilty, but have properly been found to be unfit to plead, frequently complain that they are detained without trial. How greater their grievance if capable of being tried but not allowed to do so! Are we to accept a suggestion which would avoidably deprive an insane person who is fit to plead, of his legal right if he so tried? Could injustice go further? We are sometimes told that psychiatrists do not appreciate the legal approach to criminal responsibility. Here the psychiatrist can say to the lawyers who support this proposal, that in this matter they do not appreciate the medical point of view.

This matter is of more than academic importance. Table 1 of the statistics presented to the Royal Commission on Capital Punishment by the Home Office shows that in recent years there has been a relative as well as an actual increase of persons found insane on arraignment when tried for murder. East (1950) calls attention to the fact that during the 20 years (1905-1924), when he was constantly giving evidence in the criminal courts, 127 persons tried for murder were declared to be insane on arraignment, and 325 guilty but insane. In the 20 years 1929-1948 the figures were 226 insane on arraignment, and 331 guilty but insane. It is difficult to believe that there is any psychiatric reason for this. The answer seems to be that the criteria of unfitness to plead are less strictly adhered to than formerly. But if justice is not only done, but should at all times seem to be done, it is essential to maintain the distinction between a verdict of "insane on arraignment" and "guilty but insane." Moreover, there is no appeal to the Court of Criminal Appeal from either verdict. A civil patient who is detained under certificates as a person of unsound mind does not necessarily forfeit all his civil rights. For example, he is not deprived of his right to make a valid will, if there is satisfactory evidence that he was at the material time competent to do so. He may also contest a petition for divorce. A Broadmoor patient and his relatives, bearing

* A person arraigned on indictment for any felony or misdemeanour may now challenge not more than seven jurors without cause, and any juror or jurors for cause (Crim. Justice Act, 1948, Sec. 35 (1)).

these facts in mind, may reasonably think that an accused person, although insane, ought not to be deprived of his right to be tried and defend himself whenever possible.

It is a striking fact that whereas in England and Wales 412 persons charged with murder were found to be insane on arraignment, and 783 guilty but insane during the years 1900-1948, in Scotland, during the same years, the figures were 104 insane on arraignment, and 23 guilty but insane. The evidence given before the Royal Commission on Capital Punishment by Mr. C. C. Cunningham (1950), Permanent Secretary, Scottish Home Department, shows that the insanity in Scotland which renders a man unfit to plead must be of a kind "which prevents a man from doing what a truly sane man would do and is entitled to do—maintain in sober sanity his plea of innocence and instruct those who defend him as a truly sane man would do." The difference in figures of the English and Scottish systems may reflect the difference in the criteria applied in the two countries. It may be fairly considered that the term "truly sane man" indicates a man who is mentally normal—to some observers a mythical person—and that there is ambiguity in the term "sober sanity."

Henderson (1944), East (1944, 1945) and others have contrasted the objective outlook of the lawyer in forensic cases with the subjective approach of the psychiatrist. Anyone with the necessary practical experience will agree that further progress will only result from the combined efforts of the two professions. Our aims are not opposed. Unfortunately, medical evidence regarding criminal responsibility sometimes suggests otherwise, and antagonizes lawyers and others to-day no less frequently than, say, 25 or 30 years ago. This is partly due to the partisan attitude of some medical witnesses. Perhaps still more to the fact that attempts are made to discard clinical diagnosis for psychological speculations which are often misapplied in the case under consideration, and if applicable cannot be accepted as an excuse in justice to society, although they may offer an explanation of the crime.

If we are to contribute to the much needed dignity and importance of psychiatric evidence in a criminal court we must first put our house in order.

Discussing a desirable perfection in the administration of Justice, R. D. Gillespie (1944) wrote that, to effect this judges and lawyers must be equipped with the knowledge of psychiatry and anthropology which will enable them to assess the findings and views of medical psychologists, and that the latter will have to give the same care and attention in elucidating the motives that they have given to the assessment of symptoms. MacNiven (1944), referring to the lack of specificity in the symptoms of mental disease, considers that the divergence of opinion in the diagnostic label of psychiatrists does not signify that one of them is in error. It may be that, as far as essential understanding of the case is concerned, they are in agreement, and only in their terminology different.

Our punitive measures have been evolved by the wisdom and experience of highly skilled legal and executive authorities. They meet with a large measure of success and are not static. It was almost inevitable that Lord

Cooper, Lord President of the Court of Session, Scotland, when Lord Justice Clerk (1946), found it necessary to state, in discussing Crime and Punishment, that there was reason to believe from legal journals, from a number of recent judicial decisions, and from a succession of jury verdicts in which psychiatric evidence had been repeatedly rejected, that the psychiatrist and lawyer are latterly drifting apart. He pointed out that one cause of conflict was that the psychiatrist is not used to having his opinions questioned, and the lawyer is not used to accepting other people's conclusions unexamined. McAlister (1946) refers to the criteria of responsibility in Scotland and England, and believes that in neither country can it be said that there is widespread dissatisfaction with the existing practice. He mentions that in Scotland the doctrine of partial responsibility has been accepted and applied. It, however, appears to have been overdone, and judges and juries have now come to regard such evidence with growing suspicion. Petrie (1946) states that, although a psychiatrist, he has felt sympathy for the lawyers when hearing some of the medical views expressed. Henderson (1946) supports the view that there should be two phases in a criminal trial, a guilt-finding phase and a sentence phase, the issue being determined by separate tribunals. Mannheim (1946) and others favour the setting up of a "Treatment Tribunal," and this proposal is said to have been developed in some States in America. Many persons in England may oppose this proposal unless they are fully satisfied that there are good reasons for the change. There are others who are suspicious of the number of tribunals set up in various directions to-day, and wonder what the result is going to be on personal freedom. East (1946) suggests for consideration the setting up of machinery whereby the judicial authority in grave offences, other than capital, would award a minimum and maximum sentence in each case, and a different tribunal decide when, within those limits, it should recommend to the Secretary of State that the sentence terminate, after the behaviour and mental condition of the offender, his circumstances, and prospects on release, have been reviewed.

This proposal might avoid some of the disadvantages of an indeterminate sentence, but the matter is highly controversial. Thorsten Sellin (1947) refers to the divergent opinions on the merit of indeterminate sentences in the United States of America. At the same time, he believes that this form would lead to the more effective protection of the community and a more effective reformation of the offender. Nils Beckman (1946) is also convinced of the value of the indeterminate sentence system in Sweden. Kinberg (1945) believes that administrative organs, properly composed, would be better able than the courts to decide what treatment the offender should undergo. He points out, however, that the best statutes and the best custodial institutions will fail unless the personnel in charge of the treatment are well trained. Kyhn Gløersen (1947) states that Norwegian public opinion is opposed to an extension of the use of the indeterminate sentence, and Lindberg (1947), speaking as a Stockholm lawyer, condemns the indeterminate sentence, and believes that the courts are better able to fix penalties than administrative boards.

It is sometimes suggested that since the criteria of certifiable insanity are for the most part accepted in courts of summary jurisdiction, they might also

be applied in courts of assize and quarter sessions. Although the *ipse dixit* of a medical witness may be sufficient in the less serious forms of crime, there can be little doubt that medical evidence must be substantiated to the full in cases of grave crime coming before the higher courts. Even in the courts below, medical opinions differ regarding what is certifiable and what not. Thus, a sexual offence may appear to one observer as a compulsive psychopathological state, and to another as greediness.

The Law is not irrevocably wedded to the criteria of irresponsibility as set out in the McNaghten Rules. There is no reason to believe that the Law would oppose a medical definition of irresponsibility which carried with it a verdict of irresponsibility, if it was reliable, could be understood and applied by juries, and protected the interests of the public as well as the defendant. But medicine has not been forthcoming in the matter. This was apparent in the evidence given before the Atkin Committee. Moreover, if a medical formula was accepted the Law would be entitled to insist upon a rigid interpretation of its specifications. It is not difficult to believe that hardship to offenders and embarrassment to medical witnesses would result.

Since modern psychological medicine has disclosed mental abnormalities which affect the mind less extensively than in the psychoses and oligophrenia, it has become apparent that when an offender's act is attributable to a psychoneurotic or psychopathic personality state he will often be considered only partially responsible by the psychiatrist. Weihofen and Overholser (1946) state that the only reason why defence counsel have not urged the proposition can only be surmised. They think counsel have been distracted by the tests of insanity and are therefore led to try to prove that their clients come within the test and to assume that unless they can so prove, the defence of mental abnormality is irrelevant. Very frequently in England medical evidence in murder trials is belittled because the witness attempts to prove too much. East (1944) suggests that the time has arrived when doctors can contribute more to the common good by leaving tests of responsibility to the lawyers, and by concentrating on a better understanding of the various mental conditions, short of insanity, which may be properly regarded by an experienced psychiatrist as lessening culpability, and that in order to avoid confusion we should clarify our position in these cases by using the latter word instead of the legal term, responsibility. He does not disguise the fact that one case may be hardly separated from normality, and another hardly from insanity, and that there are innumerable transitions between medical culpability and legal responsibility. With special opportunities to form an opinion he finds that the legal and executive authorities are always ready to consider clear and reasoned statements on the matter in order that justice shall be done. The authorities are often offered an overloaded statement which can serve no useful purpose. On the other hand, many will accept the view of C. K. Allen (1945) that the constant complication of technicalities which make it difficult to obtain convictions even in the clearest cases threatens to become a serious embarrassment to justice, and that there is little danger nowadays of conviction of the innocent, but that there is no small danger of the artificial innocence of the guilty.

It is sometimes suggested that different degrees of murder*—generally two—should be recognized, and that if mental abnormality is short of insanity the verdict might be guilty in the second degree, with a corresponding modification of the sentence. East (1947), from the point of view of a psychiatrist, states that even within the limits of psychiatric cases there are several degrees of heinousness and responsibility. He doubts whether a scientific grading of the many imponderables involved is possible, or capable of maintaining the present equitable balance between public safety and humanely directed clemency.

Important differences of opinion regarding criminal irresponsibility due to insanity in cases of murder have emerged during the sessions of the Royal Commission on Capital Punishment.

In his memorandum to the Commission Mr. Justice Humphreys (1949) states: "I have always understood that the McNaghten Rules apply not to the sanity or otherwise of the accused from the medical point of view, but rather to his legal responsibility for his actions." In answer to the question whether it would "be true to say that when it is clear that the accused is insane, when there is no conflict about the question, and psychiatrists and the prison medical officer called by the prosecution all agree that he is insane, that then nobody thinks very much about the McNaghten Rules?" Sir Travers Humphreys replied, "That is so. Sometimes they are not referred to. I have tried cases more than once where I have never said anything to the jury about the McNaghten Rules at all." He agreed that the Rules principally come in where insanity is disputed. And he stated that "a man ought to be hanged if he has committed a deliberate murder and is responsible in law for his actions. He must be responsible for his actions in law at the time he is hanged."

Lord Goddard, Lord Chief Justice (1949), was asked in the course of his evidence: "Do you agree with the general view that it is wrong to hang those who are insane in the medical sense?" He replied: "I think it very largely depends on what one means by 'in the medical sense.'" He referred to the case of T. J. Ley (the chalk-pit murder), who was tried and convicted before him and sentenced to death at the Central Criminal Court in March, 1947. A statutory enquiry under the Criminal Lunatics Act, 1884, section 2(4) was held on Ley six weeks later. He was found to be suffering from paranoia and was reprieved. He died in Broadmoor in less than three months from meningeal haemorrhage. In his memorandum to the Commissioners, Lord Goddard stated: "I had no doubt that the prisoner (Ley) was insane; his whole conduct, including his demeanour and evidence at the trial, showed a typical case of paranoia. But he refused to allow his Counsel to raise the defence of insanity and would have been horrified at any such suggestion. This was all part of the disease." Later in his evidence Lord Goddard was asked: "I suppose you would not have wished that man to hang? You would not think it proper that he should hang?" He replied: "I should have thought it was very proper that he should have been hanged." And

* The Parliamentary Debates (*Hansard*) on the Criminal Justice Bill make it clear that this suggestion was considered by both Houses, but was not incorporated in the Act.

when it was put to him that "the medical point of view would be that the disease had altered his (Ley's) personality so as to make such wickedness possible," Lord Goddard replied: "If that is the medical point of view, I am afraid, frankly, that it does not appeal to me at all. If that was the case, I think it is one of the reasons why he should be put out of the way." However this may be, many may find it difficult to believe that the British public are so anachronistic as to accept the view that insane offenders should be hanged.

The Lord Justice Denning (1949) suggested that "an accused person shall not be found guilty of murder unless he was, at the time, of sound mind so as to be responsible for his actions: but the test of responsibility for this purpose shall in future be that he shall be found irresponsible on the ground of insanity, not only if by mental disease he did not know what he was doing or that what he was doing was wrong, but also if the act was committed under an impulse which the prisoner was, by mental disease, in substance deprived of any power to resist." When asked "how is anybody to know whether an impulse was really irresistible, or was merely not resisted?" he answered: "That is always the difficulty which is put, but the answer is that if there is evidence of mental disease then the jury can be trusted to draw the distinction. After all, the Judge will tell them that there is all the difference in the world between an irresistible impulse and an impulse which is not resisted, and the jury will say which it is. If they had medical evidence on the matter, they would come to a conclusion which would be as satisfactory as that of the Home Office doctors."

Mr. Basil Nield, K.C., M.P. (1949), also accepted the defence of irresistible impulse in charges of murder.

The practical difficulty apparent to many against accepting the defence of irresistible impulse lies perhaps not so much in uncontested cases, where the impulse is a symptom of insanity from which the accused can be shown to suffer, as in contested cases, and particularly if the alleged irresistible impulse is unaccompanied by other evidence of insanity.

The Royal Medico-Psychological Association (1950), in its memorandum to the Commissioners, hold very strongly the view that the presence of legal as well as of certifiable insanity does not necessarily imply unfitness to plead, and that the preservation of the distinction between a verdict of "insane on arraignment" and "guilty but insane" is essential in the interests of justice. Offenders who are certifiably of unsound mind according to medical standards, as well as those found to be guilty but insane are frequently fit to plead.

The Association does not consider that the McNaghten Rules are always satisfactory from a medical point of view, but it is unable to suggest, without the co-operation of the legal profession, a suitable alternative. Until it is satisfied that there is a better formula it is in favour of the retention of the McNaghten Rules in capital cases. So long as the question of criminal responsibility is left to the decision of the jury some criterion is necessary. The Rules have the advantage of being easily understood by the jury, with the assistance of the Judge, and in this respect no satisfactory alternative has been devised. The Association considers that if the Rules were rigidly interpreted the majority of even frankly insane murderers would be judged criminally respons-

ible. It quotes Lord Haldane (1924), who stated when Lord Chancellor: "It is a great mistake to suppose that the Rules which absolve a person who does not know what he is doing and does not know the distinction between right and wrong are hard and fast rules which cannot in any way be extended in their application" (*Parliamentary Debates*, Vol. LVII, Fifth Series). The suggestion is made that the verdict authorized by the Trial of Lunatics Act, 1883, Sect. 2(1), "that the accused was *Guilty* of the act or made the omission charged against him, but was insane at the time when he did the act or made the omission," should be amended to "that the accused *Committed* the act or made the omission charged against him but was insane at the time when he did the act or made the omission."

Referring to the enquiries held by the direction of the Home Secretary under the Criminal Lunatics Act, 1884, Section 2(4), the Association states that they bridge the gap, which sometimes appears in the course of a criminal trial, between the criteria of irresponsibility according to law and the medical criteria of insanity. The doctors appointed for the purpose report not only on the insanity (if present) of the offender as assessed by medical men, but also call attention to other forms of mental abnormality short of insanity. At the same time the Association emphasizes that these enquiries do not oppose the verdict of the jury that the accused was responsible in law for the crime, but they are complementary to and supplement this finding. It recommends that a medical enquiry be ordered in every case before the death sentence is executed.

The Association declares that it cannot exclude the possible occurrence of irresistible impulses of the kinds sometimes suggested in a case of murder, but they have been impressed that very experienced forensic psychiatrists have been unable to recall a case of murder due to an irresistible impulse not associated with a recognizable form of insanity. It believes that to accept a plea that a murder was due to an irresistible impulse, when no other evidence of insanity or medical abnormality could be found, would involve the jury in obscure speculation. There is no doubt that such a plea would be liable to abuse, and impulses would be said to be irresistible because they were not resisted. Similarly, the Association believes that the conflicting opinions of opposing psychiatrists would confuse the jury if a plea of diminished responsibility was accepted. Lord Cooper in 1946, when Lord Justice Clark, stated: "But it has been overdone; and I am sorry to say that judges and jurors alike have come to regard such evidence with growing suspicion." (*J. Ment. Sci.*, 92, p. 702.) The Association considers that the question of diminished responsibility can be dealt with effectively by executive action in the review of each case that is made after trial, and that any alteration in the present practice is undesirable.

Reasonable weight is attached by the Association to the importance of the Statutory Enquiries ordered by the Home Secretary under the Criminal Lunatics Act, 1884, Section 2(4), and to the opinions expressed by the Lord Chief Justice and the Rt. Hon. Mr. Justice Humphreys, who consider such enquiries should only be applied to persons who have become insane between the dates of conviction and execution.

The British Medical Association (1950) recommends in its memorandum to the Royal Commission "the adoption of some such formula as the one set out below :

" A. To establish a defence on the ground of disease of the mind the party accused must prove that at the time of the committing of the act, he was labouring, as a result of disease of the mind, under

" (1) A defect of reason, such that he did not know

(a) the nature and quality of the act he was doing ; or (if he did know this)

(b) that he was doing what was wrong ; or

" (2) A disorder of emotion such that, while appreciating the nature and quality of the act, and that it was wrong, he did not possess sufficient power to prevent himself from committing it.*

" NOTE : (a) ' Disease of the mind ' covers incomplete mental development as well as grave disturbances of mental health.

(b) ' Wrong ' means not ' punishable by law,' but morally wrong in the accused person's own opinion.

" B. When a jury find that an accused person, at the time of the committing of the act, was labouring, as a result of disease of the mind, under a defect of reason or a disorder of emotion to such an extent as not to be fully accountable for his actions, they shall return a verdict of ' Guilty with diminished responsibility.'†

" C. In the cases envisaged in A and B above, the same burden of proof shall be upon the accused as upon the plaintiff in a civil action, and in no case shall it be necessary for a court to consider or a judge to direct the jury as to such matters unless one or other has been specifically raised on behalf of the accused."

The British Medical Association considers that the abnormal mental states in which, although the prisoner knew the nature and wrongfulness of his act, responsibility for the crime of murder may be either absent or diminished as a result of emotional disorder, include the following : aggressive psychopathic states, states associated with organic damage to the brain (epilepsy, epidemic encephalitis, etc.), depressive states with desire for self-destruction or self-punishment, early schizophrenia, paranoia and paraphrenia.

Only a few of the highly controversial matters which have appeared before the Royal Commission are mentioned here, but perhaps enough to indicate the complexities and implications involved, and the fact that different views appear between the legal and medical professions and also between individual members of the same professions.

* " It is fully appreciated that it is never possible to provide scientific and conclusive proof of a complete lack of power to control conduct at the time when a crime is committed. Since the power of control may be diminished in varying degrees, it would be illogical to exclude the possibility of it being so diminished as virtually to be absent, although in practice the cases would no doubt be rare in which a jury would be satisfied that its absence was a reasonable inference from the evidence."

† " It is suggested that it might be open, in a proper case, to a court of summary jurisdiction to record the finding of ' guilty with diminished responsibility.'"

INSANITY AND DIVORCE.

An important question recently came before the Court of Appeal (Bucknill, Asquith and Denning L. J. J.) in relation to insanity as a defence to an allegation of cruelty in a petition for divorce. Edgar Bradley refers to *White v. White* ([1949]. 2 All E.R. 339) in the *Medico-Legal Journal*, Pt. III, 1949:

"The County Court Judge, sitting as a Commissioner to hear divorce cases, had dismissed the husband's petition based on cruelty. The parties were married in 1941, when the husband was in the Army, and he had only a few days leave with his wife. He was 30 and she was 24 years old. There was one child of the marriage, born on 21 May, 1945.

"The husband, in support of his allegation, proved the following facts. Immediately after the marriage he had been sent overseas and remained there for three years. At first his wife seemed happy, but in 1943 she wrote saying that she did not want anything more to do with him but gave no reasons. Afterwards she wrote a letter saying that everything was alright, but in about June, 1944, she wrote an irrational letter which appeared to indicate that she was suffering from a delusion that someone was going to 'get her.' In September, 1944, the husband saw her, but she did not seem to know him and ignored him. She then, without any justification, started to accuse her husband of associating with other women, including her own mother. On 19 December, 1944, she went as a voluntary patient to a mental hospital, where she was soon discovered to be pregnant. Her husband took her out of the hospital and she had her baby in a nursing home. On return from the nursing home she became very difficult and would have nothing to do with her husband. The accusations of infidelity were renewed, and she refused him sexual intercourse; she neglected him and he became ill. In about the spring of 1946, because of this neglect, he left home and went to stay with his parents.

"In October, 1946, the husband went back to the house to see the baby, but his wife refused him admission and started kicking and hitting him. A few days later she left the house and went back to her parents. The husband remained in the house, and on discovering that she had failed to pay certain bills for which he had left her the money, he wrote to her. She came to the house and attacked and scratched him, using obscene language. The husband was forced to send for the police. Similar behaviour on her part continued until she finally left the house in November, 1946. She, however, behaved well when other people beside the husband were present, and made no complaint about him to them. In July, 1947, the husband filed his petition, and in December, 1947, the wife was certified of unsound mind and a proper person to be taken charge of and detained under care and treatment, and was received into the same mental hospital as she had been in previously.

"In September, 1948, the Official Solicitor on behalf of the wife, filed an answer denying the cruelty and alternatively pleading that, if she had been guilty of the alleged acts, she did not know the nature and quality of any of them.

"On behalf of the husband a medical practitioner, who had known and treated her during the relevant period, was called, who said that throughout she showed no signs of insanity. On behalf of the wife, the medical superinten-

dent of the mental hospital was called, who said that when she was first admitted, in 1944, she was suffering from schizophrenia, had a delusion of antipathy for her husband, and was then in a condition in which she might have been certified as a person of unsound mind. Her condition showed no improvement before she left in January, 1945. The superintendent said that, in his view, her condition was the same between 1945 and 1948 as it was when she was first admitted to hospital.

"The facts indicating insanity, on which the certifying doctor had formed his conclusion in December, 1947, were that she had 'bizarre hypochondriacal ideas, e.g. that something had entered her stomach and caused her to lose her grip on it, and that she should have an operation on her foot in case she met another man. Most of her speech was rambling and indirect.'

"Bucknill L. J., in his judgment after stating the facts and, referring to the Commissioner's decision, said that the question which had to be decided was whether the rule laid down in the McNaghten's case as a test of insanity was a defence in criminal cases, applied to a case such as the one before them. That rule was . . . 'to establish a defence on the ground of insanity, it must be clearly proved that at the time of the committing of the act, the party accused was labouring under such a defect of reason from disease of the mind as not to know the nature and quality of the act he was doing; or, if he did know it, that he did not know he was doing what was wrong.' In this case he understood the basis of the Commissioner's decision to be that, although in his judgment the wife knew the nature of the acts which she was doing, her knowledge was based, not on a normal, but on a diseased, state of mind, and was not, therefore, knowledge in the usual sense of the words. It seemed clear that the Commissioner considered that the test of insanity laid down in McNaghten's case did not apply in this case. It had been contended on behalf of the husband that the test whether the wife was responsible for her conduct towards her husband was the same in a petition for divorce on the grounds of cruelty as it would have been if the acts of cruelty had formed the basis of a criminal charge of injury to the husband, and that by the test laid down in McNaghten's case she would have been responsible, because all the evidence showed she knew quite well the nature of her acts and that she knew what she was doing was wrong, because she controlled herself at all times except when she was alone with her husband. On the other hand, it had been contended on behalf of the wife that the rule in McNaghten's case ought not to be extended to the case of a petition for divorce, because the rule was now regarded by scientific thought as unsatisfactory and harsh, in that it did not take sufficient account of acts done by a man under some uncontrollable impulse, an impulse which was probably the product of some physical disorder of the brain. Dealing with the facts of the case, it seemed to him (his Lordship), that the crucial question was the mental condition of the wife during the period from the time when she came home after the birth of her baby at the end of May, 1945, to the time when her husband left her and went to his parents about a year later. During this period there was no evidence of physical violence by the wife, but there was unreasonable nagging and accusations of infidelity which eventually injured the husband's health. In his view,

if the wife deliberately behaved towards her husband in a way which was not in itself quite irrational, in circumstances which indicated that she knew what she was doing and that her conduct was wrong, and if that treatment had the natural result of injuring his health, then all the circumstances seemed to him to be present to show that she treated him with cruelty. He was in favour of allowing the appeal.

"Asquith, L. J., in his judgment, agreed with the decision arrived at by Bucknill, L. J., and answered the question of what type or degree of insanity would avail a spouse charged with cruelty by saying that the inference which he (His Lordship) drew from the authorities was that so to avail, the insanity must, at all events, not fall short of such insanity as would afford a defence to a criminal charge within the McNaghten Rules. In other words, if the actor knew the nature and quality of his acts (that is to say, knew what he was doing, and knew he was doing wrong) the fact that he was suffering from a disease of the mind was immaterial, even if he would not have committed the acts complained of but for such disease.

"Denning, L. J., in his judgment, agreed with the decision to allow the appeal arrived at by Bucknill and Asquith, L. J. J., but for different reasons. In his view, if the wife had committed a criminal offence at any time after 19 December, 1944, when she was first admitted to the mental hospital, any jury would have found her guilty but insane at the time. He assumed that the jury would have been properly directed according to the McNaghten Rules, but even so, he felt sure they would have found her to be insane at the time of doing the act. Their verdict would be given under the Trial of Lunatics Act, 1883, Section 2(1), the words of which seemed almost exactly to express the Commissioner's finding in this case, namely, that she was 'insane so as not to be responsible according to law for (her) actions at the time when the act was done . . .'. In his opinion, the Commissioner's finding to that effect should not be upset. It was because he had come to this conclusion that he did not feel able to dispose of the case on the simple ground that she was not insane within the McNaghten Rules. The case raised in his mind the important question whether, in proceedings for divorce on the grounds of cruelty, insanity was a defence or not.

"In his (His Lordship's) opinion, both on principle and authority, the effect of insanity should be regarded differently in the civil courts from what it was in the criminal courts. Insanity was not, in his view, a defence to a charge of cruelty, although it might possibly be a defence where the injured party knew that the other was of unsound mind. A specific intent to injure was not an essential ingredient in cruelty, and, subject possibly to the above exception, it was no defence to prove that the wife in this case did not know the nature and quality of her acts or that what she was doing was wrong."

The defence of insanity was unsuccessful in the case of *L. v. L.*, reported in *The Times*, 27 May, 1950, as follows:

"Mr. Justice Pearce, delivering judgment in the case of *L. v. L.* yesterday granted a decree *nisi* of divorce to the wife petitioner who charged her husband with cruelty. The only specific charge of cruelty was that the husband had killed the only child of the marriage and subsequently attempted to kill himself.

The husband had been charged with murder of the child and had been found by a jury to be guilty but insane, and was now confined in Broadmoor Criminal Lunatic Asylum. The husband, by his guardian *ad litem*, denied the cruelty and alleged in the alternative that, if he was guilty of cruelty, he neither knew the nature or quality of the act, that he did not know that the act was wrong, and that he was not responsible for the act.

"His Lordship, giving judgment, said that medical evidence had shown that the shock of what had occurred had had a very great effect on the wife's health and nerves. Unless the respondent's insanity was a defence the petitioner was clearly entitled to relief, since there could be no greater cruelty to a mother than the killing of her only child. His Lordship went on to consider the numerous cases which had been cited in argument, including the dicta in *Hanbury v. Hanbury* (8 *The Times L.R.* 559; [1892] p.222) and the judgments of Lord Justice Asquith and Lord Justice Denning in *White v. White* (65 *The Times L.R.* 524; [1950], p. 39).

"It was for the respondent to establish, His Lordship continued, that a legal defence of insanity existed in matrimonial cases. It had sometimes been assumed to exist. In criminal proceedings, where the object of the proceedings was to punish the wrongdoer, such a defence was necessary in a just society, but he (His Lordship) did not think that that was a safe analogy. The function of the Divorce Court was to protect the petitioner rather than punish the respondent. Basing himself on these considerations, and on the judgment of Lord Justice Denning in *White v. White* (*supra*) he (Mr. Justice Pearce) could not find that the defence of insanity was open to the husband in this case, and he would accordingly pronounce a decree in favour of the wife.

"Solicitors, Mr. T. C. Boyes, Law Society Services Divorce Department; Official Solicitor."

SEXUAL OFFENCES.

The position regarding sexual offences in this country during World War I, estimated by the official figures for 1915-19, are significant when compared with the official figures for 1941-45, during World War II. The annual average of indictable sexual offences tried at assizes and quarter sessions during the period 1915-19 was 516, and 1,015 during 1941-45. The annual average of indictable sexual offences dealt with summarily at magistrates' courts during 1915-19 was 559, and 1,629 during 1941-45. Of non-indictable offences—indecent exposure—dealt with summarily, the figure during 1915-19 was 1,046, and 1,165 during 1941-45. Homosexual offences, with an annual average of 208 during World War I, increased to 719 in World War II.

Homosexuality.—Bennett (1947) discusses the social aspects of homosexuality, and points out that its manifestation meets with disapprobation, varying from violent condemnation to shocked surprise. Among homosexuals, as among ordinary people, every variety of character is found. Those with wide experience of the subject will know of chaste homosexuals who go through life handicapped by their disability, but fortified by the knowledge that their force of character has enabled them to forego the emotional and physical relief provided by overt expression. Bennett points out that the

doctor and the lawyer tend to deal with unstable homosexuals, and it is therefore unwise for them to generalize. He doubts if social instability is more frequent among homosexuals, as a whole, than among heterosexuals. He refers to Myerson and Neustadt (1942), who state that it is impossible to estimate the number of homosexuals. They refer to Kinsey (1942), who suggests that the number varies from over 50 per cent. of the population, and to Rosanoff (1938), who considers the proportion is 2 per cent. No systematic inquiry comparable to the well-known investigation by K. B. Davis (1929) in America among women, has been published in this country. Bennett suggests that in a matter of such importance a representative committee should be formed to collect information on the position.

Stanley-Jones (1947) stresses the importance of differentiating the condition into major groups that are variously referred to as congenital or acquired, organic and functional, physiological and psychological. He agrees that neither homosexual nor heterosexual can expect antisocial activities to pass unpunished merely because of deep-seated impulses which are said to be overpowering. Society can take little cognizance of the personal struggle between the super-ego and the id. In a former paper Stanley-Jones (1946) considers that there are cogent reasons for adjusting the operations so that a felonious assault upon a female is punished at least as heavily as a misdemeanour with a "light-hearted boy." Winner (1947) suggests that the psychological mechanism underlying male and female homosexuality is the same, though its manifestations are so different. She points out that there is every grade, from the harmless and usually quite unconscious friendships among women to the real love affair, with or without physical accompaniments. She also recognizes a second and more dangerous type of female homosexual, namely, the promiscuous Lesbian who passes from one affair to another, usually with physical relations, and sometimes causing great harm and unhappiness to others. Fairfield (1947), discussing female homosexuality, refers to the occasional tragic sequence when women have drifted into partnership, perhaps unconscious of its nature, which grows deeper and more exclusive with the passing years. If the younger woman wishes ultimately to marry, the older is left emotionally frustrated. Fairfield also refers to the tragedy familiar in the divorce courts when a previous Lesbian friendship makes a happy marriage impossible. Normananton (1947), as a practising barrister, finds that a very crude manifestation of Lesbianism in its Continental form is increasing in London. She states that although a woman might divorce her husband if he commits unnatural offences with other men, her husband has no remedy if she commits unnatural offences with other women. Legal authorities, however, have suggested that perversion in a wife might conceivably amount to legal cruelty, and the court has recently confirmed this view in *Gardner v. Gardner* and granted the husband his divorce (*Brit. Med. J.*, 20 Sept, 1947).

East (1947) calls attention to the suggestion sometimes made, that the association of other sexual perversions and other sexual activities with homosexuality is due to the fact that homosexuals are a persecuted class, and therefore tend to become associated with those who are condemned for other reasons. He believes that this is only relatively true, since the ordinary law-breaker

expresses disgust and contempt for the homosexual offender. There seems little doubt that the great majority of male homosexuals avoid arrest, and the suggestion can hardly apply to them. There is also some evidence that women homosexuals, against whom the social ban is far less strong, as a group present many characteristics to be classed as perversions and antisocial behaviour in considerable excess of those shown by a group of women whose sexuality is normally developed. East (1946) emphasizes the fact that the strength of the sexual urge, whether normal or perverted, varies in different persons. This is important medico-legally, for we do not excuse a rapist because he is over-sexed and may have more difficulty in restraining himself than many others, and it may be inexpedient to accept as an excuse for criminal behaviour the psychological difficulties of the pervert unless he is suffering also from mental disease or mental defect. Although the strength of the sexual urge, perverted or not perverted, is sometimes sufficient to cause the sexual offender to defy the penalty he may incur, many thieves and fraudulent offenders, as well as aggressive offenders, make a similar choice of action and are held responsible.

Taylor (1947) divided 96 male homosexuals received into Brixton prison in the year 1946 into four groups: pseudo-homosexuals 66; bi-sexuals 12; prostitutes 5; true inverts 13. Of the latter, seven had had psychotherapeutic treatment, in every case by a well-known psychiatrist who had contributed to the literature on the subject; three said they would resist treatment; one had been considered by a consultant at a clinic and was considered unsuitable for psychotherapy; one was too dull to co-operate. In only one was there any indication that psychotherapy would be of any use, and then only as a palliative. It seems to be generally agreed that anxiety is the cardinal indication for treatment. It will be shown by worry, shame and disgust, as well as a feeling of guilt. Curran (1947) refers to the ubiquity of abnormal sexual impulses and stresses the importance of determining to what extent individual patients can be changed. The fact that indulgence in sexual activities of any kind is associated with pleasure necessarily makes the treatment of sexual abnormalities one of particular difficulty. Curran considers that since homosexuality is an extremely frequent phase in development, and is often reinforced or maintained by special circumstances, as at school, it is unwise to make a diagnosis of constitutional homosexuality before the age of 25, and since habit formation is particularly easy in the realm of sex, the younger the patient the better is the prospect of breaking habits that are abnormal. Curran considers that a genuine change becomes less likely after youth, and is usually small in patients after the age of 25, but he thinks a good deal can be done in the more established cases by assisting the patient to bring his difficulties into better perspective and therefore be in a better position to deal with them.

Broster (1947) calls attention to the fact that the psyche does not necessarily follow the gonad, for there are as marked differences in its manifestations among intersexual individuals, when the gonads are rudimentary, as among persons who otherwise appear to be physically normal. He also states that the psyche does not necessarily accord with the upbringing of the individual. He observes that modern medical opinion has been turning more and more towards psycho-

somatic study, and that an increasing knowledge of endocrinology should tend to lessen the gap between clinical and psychological medicine.

Discussions on homosexuality usually have little to say about the victim of a homosexual attack, but the harm done to a lad must be taken into account if we are to obtain a correct perspective. Without this no one can profitably enter into the medico-legal aspects of the offence. Kefalas (1946) "simply despairs of the psychologists who can so airily dismiss the matter." He realizes that some boys are so resilient that they can carry through the experience successfully. He believes that there can be few psychologists of real experience who cannot recall tragic cases of people who have the tableaux of their minds permanently disfigured thereby, and have been hard to cure.

Exhibitionism.—East (1946) points out that conventional exposure of the body, apart from vanity, expresses a mature desire to attract an adult of the opposite sex with a view to effecting a closer relation on a future occasion. The male who indecently exposes himself adopts an immature method of attracting a young girl or woman in order to gratify an immediate desire without physical contact or long-term objective. In many cases of perversion the pervert is under-sexed and this appears frequently in exhibitionism; many are impotent in ordinary sexual relations. In men the act is usually carried out without a partner, and, especially in rural districts, is apt to cause public alarm. In women the acts of indecent exposure which come before the summary courts are not comparable to exhibitionism in men. They are incidental to sexual intercourse.

Taylor (1947) studied a series of 98 male exhibitionists received into Brixton prison, and compared his results with those of East (1924), who investigated 150 cases at the same prison. Taylor's figures showed that 53 of the cases were married, and 7 consorted with a mistress. He found that among the married men separation, domestic strife or dissatisfaction were common. East's figures showed only 57 cases were married. Perhaps the different percentages are significant in view of the fact that some workers find that the largest number of a prostitute's clients are married men who turn to her because of the indifference or aversion of their wives to the intimate relations of married life, or for some other reason. In other matters Taylor finds the variations between the two series of cases are almost negligible. Selling (1947) finds that exhibitionists usually have the belief that their potency is declining, and frequently have guilt feelings due to masturbation, and in some instances, because their wives are frigid, they have a subconscious desire to revenge themselves on the whole of womankind. However this may be, practical experience leaves one in no doubt that the actual exposure is often used as a stimulus for masturbation. Weihofen and Overholser (1946) mention that recently California, Illinois, Michigan and Minnesota have enacted laws providing for the *indeterminate commitment* to a special institution, or at least to a non-correctional institution, of persons convicted of sexual offences who are found to be suffering from psychopathic personality as distinguished from psychosis or "insanity." The institution for psychopathic criminals serving *indeterminate sentences* at Herstedvester has been established for some years. In England the principle of establishing a special institution, under the administration

of the Prison Commissioners, for the detention and treatment of non-sane non-insane offenders serving a *determined sentence* has been accepted. Post-war restrictions and other practical difficulties have delayed progress in the matter.

Foote (1944) found that stilboestrol eliminated libido, and that the effects lasted 14 days. A complete relapse with return of desire occurred 32 days after the exhibition of the drug ceased. Golla and Hodge (1949) were directed to the possibility of inhibiting libido by hormone treatment by a series of cases of acromegaly treated at the Burden Institute with large doses of oestrone. In all the male cases so treated libido had practically disappeared after a fortnight. A maintenance dose was necessary: although treatment lasted in one case for 4 years, libido returned 3 weeks after it was discontinued. These observers offered a course of hormone therapy, to abolish libido temporarily to persons whose uncontrolled urge brought them into conflict with the law, and treated 13 cases successfully. A prompt abolition of libido within the first fortnight could be effected with injections of oestradiol benzoate, 50,000 i.u. daily. In many cases it was found that if oestrone, 50,000 i.u. daily was substituted for the oestradiol injections, libido could be abolished within a month. A maintenance dose of 20,000 i.u. of oestrone orally is sufficient after the first 6 weeks. Golla and Hodge consider that treatment should be discontinued only when a restoration of libido is judged to be safe and desirable. Bearing in mind the non-mutilation of the treatment, and the ease with which it can be administered to a consenting patient, Golla and Hodge recommend it in appropriate cases.

Some persons have a genuine reluctance to accept psychotherapeutic advances to solve individual problems. In the case of some offenders psychotherapy often produces disappointing results. It is difficult to believe that any considerable number of sexual offenders would be anxious to submit to continuous oestrone treatment for an indefinite period—perhaps for the rest of their lives. There is clearly need in this direction for further research. It would be interesting to know if oestrone treatment was a useful adjunct to psychotherapy.

ALCOHOLISM.

Discussing the alcoholic criminal, Seliger and Cranford (1947) assert that no emotionally healthy individual deliberately does that which causes him to suffer, provided that he is aware that suffering will result from his behaviour. They argue that the alcoholic, therefore, is either unaware, not sufficiently aware, or does not want to be aware of the serious harmful consequences of his drinking, to do anything constructive about his addiction. Is this necessarily so? Further, is the premise acceptable? Is the drunkard's devoted wife emotionally unhealthy because she refuses to leave him?

None can say to what extent sobriety is an artificial product of post-war conditions, but the matter requires constant vigilance. Masserman (1944) found that the experimental neurosis induced in 16 cats was temporarily relieved by alcohol, and ten of the animals continued to prefer alcoholic to non-alcoholic liquids until their neuroses were relieved by various experimental

procedures. Hyde, Kingsley and Chisholm (1944) suggest that heavy drinking as an emotional outlet and form of enjoyment among the poorest classes makes outlets such as neurosis less necessary, with the result that the poorest group are no more affected by neurosis than the well-to-do. Knöös (1945) stresses the importance of differentiating true alcoholics from those who abuse alcohol. He advocates medical treatment and an open-air life as more rational substitutes for prisons in these cases. Åman (1945) holds a similar view, and Kinberg (1945) proposes that drunkenness be removed from the criminal law. Kaila (1945), on the other hand, points out that the problem is not entirely a medical matter.

The alcoholic's conflict between personal desire and social duty may be acute, but the conventions of society and public opinion must be upheld. Although criminal sanctions may appear inappropriate to some, many observers, professional and lay, may believe that the alternative disregards the right of society to be protected by the law, since medicine has no certain cure for alcoholism. Indeed, it sometimes seems that the successes attributed to apomorphine, autoserum, psychotherapy and other methods in the treatment of alcoholism are due to faith in the chosen form of therapy rather than to the merit of the particular method adopted. Carlson (1946) remarks that if the addict really desires to get over the addiction, then almost any therapy, or none at all, is successful.

Dahlberg (1942) examined statistically the records of alcoholists referred to the Official Temperance Boards in the town of Malmö. Apart from the Swedish setting it is noteworthy that those alcoholists who were sent to an institution when first reported to the Temperance Board have done better than those who were warned or put on probation. This is significant, since they may be assumed to have been the most recalcitrant cases. Dahlberg considers that vigorous rather than lenient measures should be adopted whenever possible, and that a special institution for short-term treatment gives the best results. He does not favour long periods of in-patient treatment. In his view two months is sufficient.

Ahto (1946) refers to a psychiatric investigation on 400 women alcoholic offenders from 15-20 years of age. Evidence of mental abnormality was found in 8.8 per cent. of the subjects. One-fourth could be regarded as normal. Much or very much alcohol was used by 51 per cent. Still higher percentages were noted for those who were both psychopathic and feeble-minded. Only 2.8 per cent. of those who showed no deviant characteristics used alcohol to excess. Mental deviations among the parents occurred in proportion to the incidence of abnormalities in the subjects, whether the latter group's mental defects or habits were considered. Twenty per cent. of the cases committed their crimes under the influence of alcohol, half of them were psychopaths, but none was completely free from abnormal traits. There were more abnormal individuals among the young women examined than in any corresponding group of offenders.

Bruce (1944) states that alcoholism is one of the most frequent causes of vitamin B deficiency, and that it acts by diminishing absorption through gastritis, by increasing destruction through achlorhydria, by rapid diminution

through oxidation and by diminishing the food intake with wrong choice of food. Carver (1945) states that the majority of those who become intoxicated by small quantities of alcohol show low blood pressure, low blood sugar and sexual aberration, usually homosexual in character. He suggests that it may be worth while to explore the possibility of hypersensitivity to alcohol being explained in terms of allergy. He states in a later paper (1947) that alcoholism and other drug addictions must be studied from the psychosomatic standpoint as expressing a failure of adjustment of the addict personality as a whole. Golla (1947), discussing auto-regulation of chemical equilibrium, stresses the therapeutic importance of enlarging the conception of the personality of the addict, and MacLeod (1947) suggests that investigations into the biochemistry of alcohol connects up with some of the main currents of present biochemical research, and will profit by the rapid expansion of knowledge in those fields.

Jellinek (1947) is concerned with the fact that occasionally extravagant conclusions have been attached to observations on alcoholism which relate to highly specific and small units. He points out that comparison of the consumption rates per head do not disclose the nature of the changes in the drinking habits of a nation, or a group within the nation. He finds, in the United States of America, a large consumption of distilled spirits and a small consumption of beer are together usually an indication that the drinkers are relatively few, but are heavy individual consumers. He finds no statistical evidence to support the impression that alcoholism has recently been occurring in younger people.

Newman, (1946) mentions four States in the United States of America having their own definition of alcoholic intoxication. Mamet (1945) states that no legislation has been passed in the U.S.A. providing for the compulsory taking of specimens for alcohol concentration estimation. A Bill had been proposed for presentation to Congress to require motorists in the District of Columbia, charged with operating a vehicle while under the influence of any intoxicating liquor, to submit to a chemical test to determine intoxication. Many may agree with Mamet that wide publicity of such legislation would have a marked prophylactic effect on those who drink and drive. In Sweden the police are entitled to take a blood test if they suspect that a motor driver is under the influence of drink.

Competent observers consider that an individual suspected of being under the influence of alcohol is in reality always more drunk than he appears to be, and that under the stress of violent emotion a drunken individual may, for a time at least, appear to be sober. It is also said that after emotional stress, such as may result from a road accident, the taking of a moderate degree of alcohol may cause an individual suddenly to appear drunk. These matters will be remembered when permission is asked to withdraw blood from the suspect, as the doctor may be later challenged and required to substantiate the opinion that the defendant was capable of understanding the nature and import of the request.

Forbes (1945) describes an apparatus devised to record visual and auditory reaction times. He finds that the correlation between reaction time to light and age is low and of no practical importance, and the ordinary degrees of fatigue have no effect on the reaction times. A loaded stomach influences, to some

extent at least, the reaction time to sound, the relationship being inverse, but has no effect on reaction time to light. Practice has no effect on reaction time to an ordinary stimulus, and only a slight influence on the special response to a visual signal. He states elsewhere (1947) that although there is a close correlation between the concentration of alcohol in the tissues and the clinical condition, the fact of individual susceptibility is so important that it is highly improper to establish a fixed level of blood or urinary alcohol above which an individual should be unfit to drive. He also agrees with those who think that if any blood alcohol concentration is to be accepted as absolute proof of intoxication in the legal sense, it is essential to be one at which experience has shown that no man, regardless of his inherent or acquired tolerance, would be judged clinically fit to drive a car. Such a figure would be so high that many grossly intoxicated individuals would escape detection if chemical tests alone were used. Forbes thinks that by recording the reaction times to visual and auditory stimuli, support may be given to the conclusions of the clinical examination in cases of alcoholic intoxication.

The absence of alcohol from the blood or urine may be of unequivocal value as evidence of sobriety, if a driver is charged with a motor offence.

The effect of non-narcotic drugs upon the ability to drive a motor-car may become better established as time passes. Wilder (1947) considers that patients in a state of hypoglycaemia have often been arrested as drunkards. He suggests that the marks caused by injections of insulin may be mistaken for those of a morphinist, but this seems hardly likely in this country, where the number of morphinists is few. In 1945 a defendant was convicted by the Bournemouth magistrates of driving dangerously while under the influence of a drug. He was fined and his licence was suspended for 12 months. Against this sentence he appealed to Quarter Sessions, and his counsel contended that insulin was not a drug within the meaning of the Road Traffic Act, since it was not a narcotic or hypnotic, but that even if it did fall within the scope of the Act the appellant was not liable as he was taking the drug on medical advice, and the coma from which he suffered was not due to insulin, but to the want of suitable food after the insulin had been taken. The Recorder upheld the decision of the magistrates but dismissed the case under the Probation of Offenders Act (*Bournemouth Daily Echo*, 26 June, 1945).*

CRIMINAL JUSTICE BILL, 1947, AND CRIMINAL JUSTICE ACT, 1948.

Section 4 of the Criminal Justice Bill of 31 October, 1947,† provides that if a court, on medical evidence, finds that the condition of the offender is such

* A later case may be mentioned. A man charged with driving a car when under the influence of drink, unsuccessfully pleaded illness as a defence. He admitted that he had taken some alcoholic drink that evening, but contended that it was quite insufficient in a man of his constitution to affect his driving, and that his condition when arrested was due not to alcohol but to an excess of alkali which he had taken for indigestion. The police surgeon who examined the defendant shortly after he was brought into the police station came to the conclusion that the man was drunk. A doctor for the defence saw the defendant two hours later and at first thought his condition was due to drink. He learned later that the man had been a patient of his eighteen months before, and suffered from duodenal trouble and had, but not by his advice, been taking large quantities of a proprietary alkaline preparation. He considered the symptoms were consistent with Alkalosis. (*Brit. Med. J.*, 1 May, 1948).

† The last draft of the Bill. Slight verbal alterations occur in the Act (1948) but without changing the import of the relevant passages.

as requires and may be susceptible to treatment, but is not such as to justify his being certified as a person of unsound mind under the Lunacy Act, 1890, or as a defective under the Mental Deficiency Act, 1913, the court shall have power to include in the probation order a requirement that the offender shall submit, for such period not extending beyond twelve months from the date of the order, to treatment by or under the direction of a duly qualified medical practitioner with a view to the improvement of the offender's mental condition.

The treatment required by such an order shall be such one of the following kinds of treatment as may be specified in the order, that is to say :

Treatment as a voluntary patient under Section 1 of the Mental Treatment Act, 1930, in such an institution within the meaning of that Act, or in such hospital, nursing home or place approved by the Minister of Health for the purposes of Section 1, or in the charge of such person as approved as may be specified in the order.

Treatment as a resident patient in such institution or place approved for the purpose in this Section by the Minister as may be specified in the order.

Treatment as a non-resident patient at such institution or place as may be specified in the order, or

Treatment by or under the direction of such duly qualified medical practitioner as may be specified in the order.

Except as above, the nature of the treatment shall not be specified in the order. If the medical practitioner treating the probationer for his mental condition is of opinion that part of the treatment can be better or more conveniently given at a place or institution not mentioned in the order, the doctor may with the consent of the probationer make arrangements for him to be treated accordingly. The doctor must inform the probation officer of the institution or place in which the treatment is being carried out. The probation officer responsible for the supervision of the probationer is required to carry out the supervision only to such an extent as may be necessary for the purpose of the discharge or amendment of the order.

In the history of medicine sanguine expectations regarding the value of new methods of treatment frequently become sobered by experience, and new legislation sometimes fails to effect its purpose. During the learning stages of the operation of this Act magistrates and doctors, as well as others, will be required assiduously to apply themselves to the lessons provided by its successes and failures. At first it seems likely that not all concerned will appreciate the fact that it is the offender and not the offence—the subjective aspect and not the objective facts connected with the crime—which should decide the value of this part of the Act. Too much stress cannot be attributed to the importance of careful follow-up studies of the probationers treated, and of the methods used in their treatment—psychotherapy, shock-therapy and the like.

DIAGNOSIS AND TREATMENT.

Wilder (1947), discussing sugar metabolism in its relation to criminal behaviour, believes that we are here at the beginning of a new scientific approach to the problem of crime. It may be noted in this connection that the diet in the least affluent classes in this country, and also in our prisons, contains

a large proportion of carbohydrate on account of its cheapness in comparison with proteins and fats.

Michaels and Secunda (1944) found in 122 children a positive association with electroencephalographic abnormalities when the behaviour disorder was accompanied by enuresis. Silverman (1944) interpreted the E.E.G. results in 411 male criminals, including normal criminals, psychotic and psychopathic criminals, and offenders with organic disease. The most significant observation was the high percentage (73) of borderline and abnormal patterns among the psychopathic criminals. He finds the E.E.G. is a potentially important tool in the study and management of the psychopath, but not of the normal criminal. He states in a later paper (1947) that the E.E.G. may help to solve the vexing problems of etiology, therapy and prognosis in psychopathy.

Stafford-Clark and F. H. Taylor (1949) report from the Maudsley Hospital and H.M. Prison, Brixton, London, the results of an investigation of electroencephalographic studies of 64 prisoners charged with murder. At first the selection of the subjects was governed by the wishes of the prison authorities, or of those responsible for the prisoner's defence, but in the last 2 years the subjects represented a consecutive unselected sample of prisoners on a capital charge.

Full personal and family histories were obtained from each of the 64 prisoners, as well as details of the charge and trial proceedings. They were combined in every instance with a routine physical examination, an examination of the mental state, and an electroencephalogram. Subsequently, and before the electroencephalogram records were studied at all, the cases were assessed on a purely clinical basis in the light of all the available information and grouped under 5 headings. In each case the electroencephalogram was analysed and the records grouped and compared with the results of the clinical assessment.

Group 1 (11 cases) consisted of cases in which the killing had been incidental to the commission of another crime or had been in self-defence. Cases in which harm had been intentional, as for example a blow on the head during robbery, were not included.

Group 2 (16 cases) included all cases in which it was considered that there was a clear motive for killing, or in which death followed intended violence during the commission of another crime.

Group 3 (15 cases) included those in which the crimes were apparently motiveless, or in which the motive was very slight.

Group 4 (8 cases) consisted of persons who were charged with murder in which there was a strong sexual element, only those cases were included in which sexual activities of some kind occurred actually at the time of murder.

Group 5 (14 cases) consisted of persons who were found unfit to plead or guilty but insane at their trials, or were subsequently found to be insane at a Statutory Enquiry. The results were as follows:

E.E.G.	Group.					Total.
	1.	2.	3.	4.	5.	
Normal	10	12	4	4	2	= 32
Mild unspecific	..	2	5	3	7	= 17
Severe unspecific	1	..	4	..	2	= 7
Specific, local or epileptic	..	2	2	1	3	= 8
Total	11	16	15	8	14	= 64

The authors consider "that in the E.E.G. we possibly have at least an objective indication of innate propensities affecting responsibility—an indication moreover which is likely to be of maximal value in precisely those cases where clinical observation and the operation of reason are least able to elucidate the basis for the individual's action—is one worthy of consideration." They add that "these cases may display no clinical evidence of insanity—either legal or medical—whatever, yet unless, as seems highly unlikely, the correlation between apparently motiveless violence and an abnormal E.E.G. is purely coincidental, they are the very subjects who most of all require further investigation and study over a prolonged period, as well as detention for the protection of the community."

In a recent memorandum Denis Hill states :

"Changes in the electrical patterns of the E.E.G. relate most directly to the physical and chemical activity of the brain cells, to the individual's state of conscious awareness, less to the personality of the individual, and in no known way with his thoughts and emotions. The patterns at the time of the examination demonstrate the functions of the brain, in the above terms, at that time and do not, in themselves, give any indication of those functions at any other time. Thus, the record may, for example, demonstrate that the individual is subject to epileptic seizures, but obviously does not prove that he actually suffered from a seizure at any given time in the past. Again, the E.E.G. data may suggest that under certain conditions the subject would suffer from a degree of dazing or 'clouding of consciousness,' but the above data cannot indicate that such actually occurred at the time of any alleged crime."

Particular caution is necessary in situations where questions of medico-legal responsibility arise. A young man, aged 21, strangled the girl he was courting against the wishes of her parents. He gave a clear account of the crime to the police. The E.E.G., taken on two different dates in the same week, showed a focus of abnormal potentials, probably in the posterior and upper part of the left frontal lobe, and raised the possibility of a structural lesion of the brain near the area of the focus. A neurologist was unable to detect any other indication of abnormality in the nervous system, and examination by three psychiatrists showed no evidence of psychosis, psychoneurosis, psychopathic personality or mental defectiveness. The post-mortem showed no macroscopic lesion of the brain, and sections taken from the right and left frontal lobes showed no microscopic abnormality.

Karpman's (1944) analytical studies in the psychogenesis of crime encourage the hope that other psychotherapists will publish more frequently their successes and failures in the treatment of criminals. Follow-up studies are badly needed in order to assess on a large scale the value of psychotherapy in this field. Lindner (1945) claims to have benefited the style of life of a delinquent boy with the aid of hypnoanalysis. He considers (1947) that intramural investigation on criminals can be aided by this method. Greenacre (1947) believes that the psychopath generally cannot be psychoanalysed. Blackman (1947) states that individual psychotherapy in prison eases the inmate through periods of emotional stress without letting him escape entirely into a

state of dependency, and he thinks that group psychotherapy helps to develop adult social patterns. East (1946), Mackwood (1947) and Young (1947) consider that the results of psychotherapy in prisons is encouraging in selected cases. The results of individual and group therapy carried out by Mackwood, Gould and others in English prisons should prove instructive.

In an important paper J. C. Mackwood (1949) considers the psychological treatment of offenders in Wormwood Scrubs Prison. He finds the unbiological setting of prison conditions operates unfavourably for satisfactory testing out of gains, though it must be stated that these same conditions, with the impossibility of retreating still further from facing up to reality, often operate favourably in the analytical approach. This is demonstrated by the increased tempo with which cases respond compared with similar cases treated under civilian conditions; and also by the fact that some who had declined or broken off treatment outside prison faced up to it inside. He considers it is possible to start the socializing of anti-social offenders in prison, and to effect very good changes up to what might be termed cure, toward enabling them to take their place in the community. He recognizes the disparity between activities and opportunity in prison, and what is open to the ordinary citizen. He points to the fact that absence of opportunity is absence of temptation, and the prison regime itself is a support inducing dependence, once the offender settles down and accepts it, even when he is co-operating. This disparity needs further bridging, and needs more elasticity from inside so that offenders can be tested out in conditions more nearly resembling those outside in the community. It also needs in greater degree the understanding and good will of the community, and the provision for the taking over of the discharged offender from the moment he goes outside. Mackwood appreciates the fact that some of the newer prisons are definitely a step in this direction, and that on the whole much more has been done from within prison walls than has been done by the community outside. He believes that however much is done from inside it will be largely wasted unless the general public is educated away from its retaliatory attitude to offenders, and from the idea that punishment is the main deterrent for delinquency and crime.

The value of prefrontal leucotomy as a practical method of treatment in some cases of mentally abnormal offenders is a matter for future research. The Board of Control (1947) finds no present answer to the question whether the beneficial results so far are, or are not, achieved at the cost of the loss of some finer mental qualities. Hutton (1947) considers that the undesirability of the post-operative personality seems much more definitely allied to the character of the patient prior to his illness than to the form of illness to which he succumbed. It is difficult to believe that the operation can be justified in cases of accidental or occasional criminality. The habitual criminal is already antisocial, and to risk reducing by operation any remaining socially acceptable trends may be, perhaps, calamitous in our present state of knowledge.

The importance of narco-analysis as well as shock-therapy, and perhaps prefrontal leucotomy in the prevention and treatment of crime awaits further exploration. But caution is necessary. A shock-treated schizophrenic recovered sufficiently to obtain his discharge from a mental hospital, but not

sufficiently to prevent him later from committing a schizophrenic murder. Disappointments are almost inevitable, but we may believe that psychiatric methods of treatment applied to some mentally abnormal offenders will repay further investigation.

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SLEEP AND ITS DISTURBANCES

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INTRODUCTION.

It used to be the practice to preface every article on sleep with regret that although nearly a third of one's life-time is spent in sleep very little is known about it, in spite of many elaborate experiments conducted with a view to determining its various aspects, e.g., the so-called depth of sleep and the effects of partial or prolonged wakefulness. The various phenomena occurring during states of apparent sleep had also remained obscure; there was also a universal belief that insufficient sleep over a long period probably caused incurable insanity and so on.

The recent global war has, however, provided ample opportunities on an unprecedented scale for studying every aspect of sleep, its disturbances, the effect of lack of sleep and the various phenomena occurring in the borderland of sleep, i.e. the transitional period between complete wakefulness and sound sleep. The carefully obtained laboratory findings pale into comparative insignificance beside the mass experience of the war years involving millions of human beings of both sexes and of all ages; the knowledge thus acquired may, indeed, rightly be claimed as one of the major psychiatric gains of World War II.

For nearly six years in Greater London with a population of eight millions, and in many of the larger cities, the sleep of the vast majority of the population was disturbed almost nightly—either by the frequent sounding of the siren announcing approaching enemy aircraft, or, by actual air raids often followed by bomb explosions. Hospital in-patients suffering from organic illnesses—both medical and surgical—as well as those afflicted with psychoses and neurosis were frequently awakened at night and sent to air raid shelters.

Undisturbed sleep was almost unknown for personnel engaged in the various combat zones in land warfare; survivors of ships torpedoed at sea and clinging to life-boats or wreckage were also deprived of sleep for prolonged periods.

Nevertheless, neither clinical, statistical or other evidence has been forthcoming to shew that even an appreciable number of normal persons have suffered any physical or mental disability which could be directly attributed to the effects of insufficient sleep. In the United Kingdom, during the war period, the total number of psychotic patients in mental hospitals was actually smaller than before the war and the number of new admissions per year was again smaller than the average for the pre-war years; further, among civilians there was no increase in the incidence of neurosis either (Jones, 1945).

The war years have, therefore, indicated a possible new line of approach in the study of the minimum number of hours of sleep necessary for mankind. Primitive man slept during the hours of darkness; with better methods of in-door lighting the hours devoted to sleep gradually got fewer until it was

generally accepted that for an adult about eight hours were necessary to maintain optimum physical and mental health. But these eight hours of sleep appear to have been accepted as desirable without any really valid physiological basis. One of the lessons of the war has been to emphasise that most people can manage on as few as five or six hours or less of sleep without any serious detriment to their health.

Unfortunately, owing to paper shortage in Great Britain, editors of medical journals were temporarily obliged to accept short articles and those of urgent topical importance only. This in part explains the scarcity of contributions on the subject published in this country ; nevertheless, at meetings and discussions of learned societies, physiologists and psychiatrists have been able to pool their experiences. The various methods of inducing narcosis, the extensive use of barbiturates given intravenously for purposes of abreaction, and hypno-analysis and hypnotherapy have enabled psychiatrists to study the clinical features and psychological manifestations accompanying the various transitional stages between full wakefulness and deep coma. This study has thrown much light on such common sleep-disturbances as talking, walking, dreams and nightmares and so on.

Another factor which has helped to elucidate doubtful points and to confirm clinical findings has been the service rendered by psychiatric social workers and after-care officers, who, by obtaining information from independent sources have often supplied many of the key pieces in this human jigsaw puzzle. The correspondence columns of both the medical and lay press as well as evidence tendered in juvenile and other law courts has also assisted in the formulation of somewhat clearer views on hitherto obscure phenomena associated with sleep dysfunction. Knowledge thus gleaned from the hot cataclysm of war is likely to be of greater practical use than cold conclusions drawn from the laboratory experiments whether on animals or humans.

On the basis of available evidence it may be emphatically stated that the various vocal, motor and psychic (problem-solving) activities which were supposed to occur during sleep actually result from varying degrees of consciousness. Some of the so-called somnambulistic actions give clear evidence of spatial orientation and unimpaired lucidity of memory compatible with complete wakefulness.

Some of the papers published during the period under review have been characterised by careful observations, patient team work and guarded conclusions which record outstanding advances in neuro-psychiatry. Some writers have given excellent reviews of the theories on the nature of sleep and a few have summarised the earlier literature on narcolepsy. As the psychoanalytical contributions do not record any definite advances only a few will be here reviewed.

Definition.—Brain and Strauss (1945) state that during sleep *consciousness is lost*. It is difficult to accept this statement since a person who is unconscious cannot be easily roused by ordinary stimuli and even when awakened by strong stimuli may not appear to be in complete possession of his senses. This is not the case with normal sleep, during which a person may be roused easily and when awakened appears to be in complete possession of his faculties. A

definition which also fits in with the wartime experience of thousands of night-shift workers, A.R.P. officers and others is that sleep is a periodic, complex physio-psychic state involving *dimming of consciousness*, usually relaxation of skeletal muscles and temporary changes in the sensory-motor functions (Pai, 1946b).

PHYSIOLOGICAL STUDIES.

Relaxation and Posture.—As mental activity is invariably accompanied by physical activity, complete physical rest necessarily includes mental rest. Jacobson (1944) insists that there is no laboratory evidence for supposing that mental rest is opposed to physical rest. When muscular relaxation is incomplete mental activity and emotional states persist. It is therefore not surprising that a person who has not slept most of the night often complains of feeling more tired than when he retired to bed. The final stages of progressive relaxation count most in ensuring restful sleep. According to McDonnell (1946) many symptoms and painful disabilities such as intercostal neuralgia and so on result from a faulty sleep posture assumed by a large proportion of the population who do not know how to lie in bed. The correct posture for sleep is that of lateral recumbency with the overlying knee on the mattress and external to the underlying limb. He disagrees with the concept of psychosomatic rheumatism and expresses the view that the muscle and joint pains which awaken patients at night are not due to dream imagery as psychiatrists often think but to mechanical causes resulting from incorrect sleep posture. Rotation of vertebrae, a widening of the costovertebral ligaments, and irritation of intercostal nerves are responsible for many painful disabilities.

McDonnell's views are not supported by the experience of thousands of Londoners who, during the war, slept in overcrowded underground railway stations and air raid shelters. There has been no statistical evidence that the incidence of painful disabilities has appreciably increased as a result of the faulty posture assumed by these people.

Motility.—As a person who changes his position during apparent sleep is half-awake it is desirable to determine objectively the motility when he is ostensibly asleep. Kleitman (1944) points out that movements during sleep may be measured either by mechanical means or by establishing pneumatic connections between an inflated bag under the mattress and a recording tambour in an adjoining room. An apparatus developed in Kleitman's laboratory enables one to determine the total time spent in motion. Distribution of movements through the night can be ascertained by using a slow-moving kymograph. A photo-electric arrangement can be used without any recording system. From the record it is possible to ascertain not only frequency of movement but also to count major and minor movements. The electric clock readings give the time spent in movements in seconds per hour of sleep. Curves of the depth of sleep are actually statistical representations of the variations of one or another concomitant of sleep. Depending on the concomitant chosen the greatest depth of sleep may be in the late hours of the night or in the early hours of the morning. After about two hours motility is minimum and therefore the depth of sleep maximum.

Depth of Sleep.—This is of particular interest to psychiatrists, since the action of hypnotic drugs can be assessed by ascertaining the depth of sleep. Kleitman (1944) points out that depth of sleep may be measured by an auditory stimulus delivered by a magnetic loudspeaker connected through a rheostat to a 100-V a-c outlet. When a patient complains of insomnia, the curve of the onset of sleep can be prepared before and after the hypnotic dose has been given. Tests may be repeated during the night to determine the depth of sleep and compared with the patient's statements. Motility during sleep has a reciprocal relationship to depth of sleep.

In an attempt to determine the average length and depth of sleep, Cohen (1944) interrogated a group of 500 young women whose average age was 21. Each was asked four questions and the replies accepted without further scrutiny. He found the average duration of sleep was 8 hours. Similar questions were put by Chrysanthis (1946) to 1,418 pupils whose written answers were obtained in the class room in the presence of the teachers! The objections to these methods are so many that they are hardly worth discussing.

Gaylord and Hodge (1944) studied the duration of sleep induced in normal and castrate female rats by giving subcutaneously 30 mg. of pentobarbital per kilo of body weight. The normal rats slept twice as long as the castrated ones. When both groups were exposed to higher temperatures all the rats showed a tendency to sleep for shorter periods. The conclusion is drawn that cases of barbiturate poisoning might benefit from fever therapy.

Gastric motility and muscular twitching.—There is a popular belief that dreams and nightmares are often associated with or result from indigestion. From a study of simultaneous records of body movements during sleep and hunger contractions Wada had concluded that strong contractions of the stomach either synchronised with or accompanied body movements occurring during dreaming periods. McGlade (1942) has conducted a series of experiments on three persons out of 25 tested, whose sleep records showed that they were subject to peculiar twitchings of the right foot during sleep. A crystal microphone strapped to the chest directly over the region of the pylorus and connected to a high-gain amplifier enabled the movements of this sphincter to be studied during wakefulness and during sleep. During waking hours the sphincter opened quietly, and as the partly digested food flowed into the duodenum the sound became fainter and fainter until it ceased altogether. When the subject fell asleep with food in the stomach the abrupt opening of the sphincter and the rapid passage of food caused a sharp snapping sound followed by a quick rumbling sound. The subject was given an ordinary meal before 6.30 p.m. and test food was given before 11 p.m., when the subject retired to bed. Movements of the foot were observed at onset of sleep soon after retiring to bed. When roused immediately after the cessation of the foot twitches, the subject was able to narrate an incomplete dream. McGlade says a dream was invariably recalled on the morning following the appearance of each group of foot twitches. In each instance the group of 20 to 50 foot movements ceased about three hours after the onset of sleep. There was a definite time interval between the food intake and the occurrence of movements.

Each twitching was almost synchronous with the sound of the relaxing sphincter. A dream was also remembered and seemed to have been experienced at the termination of the series of twitches, and it coincided with the sounds of the sphincter suggesting the complete evacuation of the stomach. Whether a dream is to be experienced or not is determined by the type of food in the stomach at the time of retiring to bed !

Circulatory System.—It is well known that during sleep the heart rate slows down, but its lowest value is reached only during the second half of the night (Kleitman 1944). Henry (1942) has found that the heart rates both at rest and after exercise were lower after a sleepless night. A cardiometer was used by Jackson (1942) to determine electrically the heart rate and a moving strip of paper recorded each heart beat along with the movements of the sleeper. The onset and termination of each movement was determined by means of a high-speed kinetograph. Jackson analysed the records for twelve complete nights' sleep of one subject and studied the larger movements involving a change in position of the trunk. He found that as much as six minutes before body movement took place the heart rate commenced to rise slowly and increased steadily until there was a rapid rise immediately before movement. On completion of movement there was a slow return to the previous rate. According to a statistical analysis of the data both the anticipatory increase and the following decrease were found to be reliable. Jackson maintains that these data provide confirmatory evidence of the so-called congestion hypothesis. Earlier Johnson had expressed the view that during sleep there is an overheating of the unventilated portions of the skin which by acting as an irritating stimulus leads to a change in body position.

Casas Carnicero (1944) has investigated the blood picture during sleep in young volunteers who were convalescing from various diseases but whose general condition was otherwise good and who could be regarded as normal. From each subject four samples of blood were taken from the finger-tip on four different days at 7.30 p.m., 11 p.m., at 3 a.m. and at 9 a.m. The afternoon samples were taken on the first day and the morning samples on the next, and the night samples were taken on two consecutive nights. The blood picture during sleep was of a vagotonic type with a diminution in the number of red blood corpuscles, leucocytes and platelets. The decrease in the total leucocyte count was caused by a diminution in the number of neutrophils, whereas the lymphocytes remained unchanged or showed a slight increase. During sleep two types of curve were found for the changes in the blood picture. In the first the changes were most marked in the early hours of sleep and in the other these changes did not occur until the early hours of the morning. Frommel et al (1947) have found the cholinesterase activity of chicken blood obtained by decapitation was considerably greater than that of blood obtained from the vein during life. The cholinesterase activity of serum decreases 10-40 per cent. during physiological sleep. Foltz, Jung and Cisler (1944) have reported slight negative correlations between total work output and an estimate of feeling tone ($r = -0.12$) and hours of sleep ($r = -0.25$).

The Excitability of the Respiratory Centre.—By employing a modification of the method described by earlier workers Ostergaard (1944) has investigated

the excitability of the respiratory centre in human beings during the waking state, and during spontaneous sleep as well as during evipan sleep and during evipan anaesthesia. After the subject had been exposed to mixtures of air and CO_2 in varying proportions the corresponding values for alveolar CO_2 tension and the changes in ventilation were determined. When these were plotted with the alveolar CO_2 tensions (in mm Hg) as abscissa and the ventilation (in litres per minute) as ordinate the steepness of the resulting curve gave a measure of the excitability. Two experiments on spontaneous sleep were made in the evening at normal bed time. One subject who fell asleep before the start of the experiment breathed in a mixture of air and 4 per cent. CO_2 . During sleep there was a decrease in ventilation amounting to 20 per cent. The second subject fell asleep after breathing the CO_2 mixture for 20 minutes. At onset of sleep there was a decrease in ventilation indicating that the excitability of the respiratory centre was reduced during sleep.

In a second set of experiments sleep was induced by giving intramuscularly a freshly prepared 10 per cent. solution of evipan. Preliminary experiments were made on two subjects who were exposed to mixtures of air and 5.6 per cent. CO_2 . When ventilation had reached the maximum limit one subject was given 0.5 gram of evipan and the other 1 gram. Sleep set in about 10 to 14 minutes after the injection. The fall in ventilation (34 per cent.) was greater in the case of the subject who had received the larger dose of evipan. In another experiment the subject was aroused from a deep and restful sleep induced by evipan and kept awake for a time. During this period the ventilation rose to a level slightly higher than the waking value before the evipan was given. When the subject was allowed to resume sleep there was again a fall in ventilation. Three confirmatory experiments were made by giving evipan in hypnotic doses. The subject was given evipan and asked to keep awake and do some simple calculations. During this period there was no appreciable fall in ventilation. But as soon as the subject was permitted to fall asleep there was a sudden fall in ventilation (34 per cent.) which remained more or less constant. When however the subject was aroused and kept awake the ventilation rose to a little above the normal waking value. These experiments would indicate that it is not the size of the dose nor the action of the hypnotic drug but the state of sleep which depresses the excitability of the respiratory centre.

Eight experiments were made on four subjects by giving evipan in anaesthetic doses to produce light anaesthesia (dulling of sensation to pinprick) except in one subject who was examined in a state of deep anaesthesia. It was found that the fall in ventilation was much greater (48 to 80 per cent.) during anaesthesia than during sleep. The decrease was directly proportional to the depth of the anaesthesia, i.e., to the concentration of the drug in the blood. Sudden overdosing might cause respiratory paralysis. This action of evipan when given in anaesthetic doses is in marked contrast to its action when given in hypnotic doses. According to Kleitman (1944) the partial pressure of carbon dioxide in alveolar air (and its tension in the blood) reaches the maximum value only about an hour after the onset of sleep.

Electrical Resistance of the Skin.—The electrical resistance of the skin indicates the activity of sweat glands and therefore also of one of the functions

of the autonomic nervous system. From previous investigations and the findings of earlier workers it may be assumed that it is the insensible perspiration which is expressed in the electrical resistance curve of the skin during sleep. Regelsberger (1942) considers that the electrical resistance curve of the skin to direct current generally shows the time of falling asleep and the time of awakening clearly, but it is only roughly parallel to the degree of loss of consciousness. This curve is the expression of a vegetative change taking place in the heat regulating mechanism and is in contrast to the usual inhibition of the sweat glands during sleep. The diminution of this resistance during sleep indicates a sympathetotonic effect of the cutaneous vegetative nervous system. The innervation of the insensible perspiration is two fold—a rhythmic component from the sympathetic chain and a tonic component conducted by the parasympathetic by way of the posterior nerve roots. Regelsberger expresses the view that the change in the vegetative nervous system associated with sleep takes place within the framework of a rhythmical process under cerebral control, which also includes the diurnal variations of the so-called electrodermatogram. The electrical resistance of the palmar skin reaches its maximal level at the beginning of the last third of the night's sleep (Kleitman 1944). By the use of "adhesive electrodes free from pressure" Regelsberger (1942b) has confirmed his earlier finding that the electrical resistance of the skin is diminished during sleep. With this method the resistance to direct current showed shorter rhythmical variations corresponding to similar variations in the alveolar CO_2 . Regelsberger considers the parallel course of these two very different processes may be due to what Pavlov called "inductive coupling" of the two centres regulating respiration and insensible perspiration. The increase in the latter during sleep indicates the excretion of additional amount of water through the skin. During waking hours this additional water is dealt with by the pulmonary ventilation. The oral administration of hypnotic drugs causes a rise in the level of the resistance curve of the skin of the lower half of the body.

Ryan and Ranssen (1944) have reported that after sleeplessness the electrical resistance of the palmar skin was unusually high.

Temperature.—The body temperature, as Kleitman points out, is unquestionably the outstanding factor in the sleep-wakefulness cycle. It is both the cause which initiates many physico-chemical processes in the body as well as the result of such processes. Its lowest level is reached about the middle of the sleep period.

Brain Metabolism.—Richter and Dawson (1948) conducted some experiments on rats to determine the biochemical changes in the brain during sleep and also during emotional excitement under normal conditions. These animals were killed by immersion in liquid air and the lactic acid content of the whole brain was estimated. In 10 normal rats killed in the resting state the brain lactic acid level ranged from 13.4 to 24.4 mg. per cent. with a mean of 18.8. The lower values were found in animals which were dozing at the time of their removal to liquid air and the higher values in animals which were wide awake. In six sleeping rats the mean lactic acid was 12.2 mg. per cent. Emotional excitement (anger and fear) was caused by allowing 11 rats to drop from side

to side in a glass beaker. The brains of these rats yielded a higher content of lactic acid ranging from 24.2 to 50.3 mg. per cent. with a mean level of 37.5, indicating a relatively high rate of metabolic activity in the brain. This increase was not due to muscular activity as a similar rise was also found in animals immobilised by tubocurarine. Muscular exercise in trained animals was not followed by a rise in brain lactic acid. Richter and Dawson conclude that emotion causes a transient rise of lactic acid in the brain which returns to normal when the excitement ceases.

Electrical Activity.—Bakuradze and Narikashvili (1945) studied the electrical activity of the cerebral cortex during normal sleep in ten men aged 18 to 40 years. A Messerschleif oscillograph recorded two cortical regions every 10 to 20 minutes. During the drowsy state the alpha-rhythm recorded from the occipito-parietal and temporal regions at first decreased and then became irregular and finally with deepening sleep this rhythm disappeared altogether. When sleep developed gradually the alpha rhythm decreased and was then replaced by weak and irregular potentials. When sleep became rapidly deep the alpha rhythm disappeared without a preliminary decrease. The occipito-parietal and temporal regions recorded periods of weakening and silent periods lasting sometimes till awakening.

The replacing of alpha rhythm by basic activity potentials was more marked in the frontal and central regions. A progressive increase in the irregular potentials of basic activity was noted from the commencement of the drowsy state. As the basic activity in the anterior half continued to increase the alpha rhythm in the posterior half continued to decrease. During sleep although the alpha rhythm decreases the electrical activity does not cease altogether. The basic activity which sets in earlier not only replaces the alpha rhythm but may become regular consisting of delta waves and spindles. This basic activity is more marked in the anterior part of the brain. Symmetrical regions of both hemispheres recorded similar potentials which followed a synchronous course.

The progressive increase in basic activity with the deepening of sleep is thought to be due to decrease or absence of afferent impulses from different receptors especially proprioceptors. This study supports Kleitman's theory of the nature of sleep.

The effects of various drugs on the electrical activity of the cortex of unanaesthetised cats has been studied by Bremer (1943). Ordinarily stimuli cause a primary positive (spike) wave succeeded by secondary waves. Natural sleep and barbiturates in hypnotic doses were found to depress the secondary waves. The amplitude of the primary wave was increased and the secondary waves much depressed or abolished by giving larger doses of barbiturates. Both the primary spike and the secondary waves were affected by ether.

Induction of Sleep.—Some of the changes in volume and composition of blood during sleep actually commence after lying down for a few minutes. It is known that during sleep the urine output is decreased and the blood diluted. Severe muscular work which often hastens the onset of sleep causes a diminution in the output of urine. Some of the diuretic drugs like caffeine cause wakefulness. These considerations led Schütz (1944) to think that the

internal milieu which exists during sleep might possibly be brought about by the simultaneous administration of the antidiuretic principle of the posterior pituitary and water. Schütz made experiments on hospital patients who were unaware of the object of the procedure. Ten to 15 units of oxytocic preparation and 1 to 2.5 units of the presser principle were divided into two doses and given by injection at 11 a.m. and at 12 noon. One and a half to 2 pints of water was given orally. The second injection was followed by lunch and from 2 p.m. onwards the subjects remained in bed. Of 24 patients 13 slept for long periods, five did not sleep longer than usual and the remaining did not sleep at all.

In another set of experiments 11 patients were given 1 per cent. saline instead of water. Five slept longer than usual, three experienced pronounced drowsiness and three felt no effects at all. Sleep induced by this method was reported to be very deep and dreamless. Eight subjects were given either the injections only or the water only with inconclusive results. It is difficult to say whether the increased depth and duration of sleep was the result of the antidiuretic principle or of the oxytocic principle or of both.

On the question of inducing sleep it is well known that many Eastern peoples have several methods of doing this without the use of drugs. One of these measures practised by some Balinese sorcerers has been described by Schlager and Meier (1947) and consists in applying manual pressure in the region of the carotid sinus. One of the authors who allowed himself to be put to sleep by this method experienced visual disturbances and a feeling of strangulation before he lost consciousness. These effects are believed to be due partly to cerebral anoxia (Smith 1948) and partly to stimulation of the carotid sinus receptors. In the remote villages of India cases of maniacal excitement which fail to respond to large doses of hypnotic drugs are sometimes put to sleep by this method, which deserves further study.

Kernodle, Hill and Grimson (1944) have described an experimental technique for measuring mean systolic blood pressure during activity, rest and sleep, while Kernodle (1946) has studied the effects of natural sleep on blood pressure of renal hypertensive dogs. There has been no unanimity in the observations of blood pressure of sleeping human beings as nearly every one of the automatic devices for recording the blood pressure readings was found to disturb the sleepers. The behaviour of haemoglobin saturation during sleep has been investigated by Allella and Meda (1946) and King (1946) has published the results of electrometric studies.

EXPERIMENTAL STUDIES OF WAKEFULNESS.

Induced Insomnia.—No significant physiological or biochemical changes have been reported in adult human beings during forced wakefulness even up to 160 hours. Henry (1942) has investigated the effects of experimental insomnia in eight male students whose ages ranged from 20 to 21. Twenty-four hours of sleep deprivation produced no changes in the systolic, diastolic or pulse pressures on change of posture, e.g., standing, reclining. The mean heart-rate was lowered while resting in the horizontal position and also during exercise and

recovery. When a modified Valsalva's experiment was performed during early recovery from exercise there was a reduction in the amount of bradycardia. The heart rate was not lowered while standing. Henry thinks that some part of the normal mechanism responsible for controlling the heart rate towards the end of exercise and during recovery becomes less sensitive as a result of sleep-deprivation. Results with cardio-vascular functional test scores were interpreted in the light of sleeplessness. Deprivation of sleep causes a lowering of the pulse rate during exercise and the later stages of recovery.

Slight psychomotor changes such as slower reaction time and inability to persist in effort and performance may occur during forced wakefulness. Tyler (1947) subjected some military and civilian volunteers (whose ages ranged from 17 to 35) to strenuous physical activity with only short intervals of rest during which they were not allowed to lie down. Amphetamine was given in 10 mgm. single doses or 5-10 mgm. in repeated doses. Barbiturates were given every 12 hours. Sixty-three men completed experiments of 24 hours duration, 81 men of 48 hours, 169 subjects of 60 to 72 hours, and 275 of 112 hours. On completion of the experiments they were allowed to sleep. During the period of wakefulness and after awakening from sleep they were subjected to a series of tests designed to measure fatigue of the central nervous system. The tests included the "body sway" with eyes closed, vibration sense, flicker fusion frequency, marksmanship, and multiple choice reaction time and so on. Muscular fatigue was assessed by the ability to perform forced marches, etc. Changes in mood were also observed. The effect of amphetamine in improving performance appeared to be due to its power in preventing sleep. In tests of long duration, when amphetamine was given at a time to cause wakefulness it prevented the falling off in performance and also caused increased attentiveness. Difficulty in staying awake rather than muscular fatigue was responsible for the inability to sustain effort. Marked but transitory psychological disturbances were observed in some men subjected to prolonged sleeplessness.

The mental disturbances, such as increased irritability, inattention, loss of memory, general indifference and even occasional tendencies to hallucinations and illusions, which may occur after sleeplessness are to some extent dependent on constitutional and personality factors. As the EEG findings during sleep are constant and reliable Tyler, *et al.* (1947) decided to study the qualitative changes in the EEG during forced insomnia. Twelve men whose ages ranged from 18 to 33 years were divided into three groups of four men each. Control recordings with the subject seated, eyes closed but awake were taken three days prior to the experiment. During the experimental period records under exactly similar conditions were taken on one group at 50 hours, on another group at 75 hours and on the third group at 100 hours of forced wakefulness. It was found that the rate of the potential changes in the brain increased progressively as the period of experimental insomnia was prolonged. In another set of experiments the effect of mental arithmetic on the per cent. time frequency distribution was studied in four different periods, e.g., the resting period, the pre-problem period, problem-solving period, and the recovering period. Mental activities caused a progressive increase in the rate of the electrical rhythm. The authors

claim that EEG records when analysed on the basis of per cent. time frequency distribution provide an accurate method of studying the effects of mental activity, as the changes in electrical rhythms which occurred were regular and the increase was proportional to the intensity of the mental work. Mental effort during the period of induced insomnia resulted in irregular changes. It appeared that a brain already fatigued by sleeplessness was unable further to increase its rate of electrical activity in response to an additional mental effort. Both prolonged wakefulness and mental effort produced the same qualitative changes namely, an increase in the rate of the electrical activity of the brain.

Licklider and Bunch (1946) conducted experiments on rats, which normally sleep 12 to 15 hours a day, with a view to determining the minimum amount of sleep required and the effects of total deprivation of sleep for short periods. When four groups of rats were kept awake 12 hours, 16 hours, 20 hours and 24 hours a day respectively, the animals were found to adjust themselves reasonably well on four hours a day for sleep. As a result of total deprivation of sleep the rats became first irritable, then aggressive and a few definitely vicious. All fell behind in weight, a few grew scrawny in appearance, and some rapidly lost weight and died. In another set of experiments the effects of partial deprivation of sleep for long periods on the maze-learning ability was studied. The wakeful rats were more vigorous, swam faster and in all of the measurable aspects of maze performance were superior to the controls. The former needed fewer trials and made fewer errors. This superiority was considered to be due to better performance and not to better ability to learn. The authors conclude that enforced wakefulness as well as solitary confinement without exercise led to improved maze performance, although the improvement was more striking after enforced wakefulness.

Hypnotic Trance and Wakefulness.—It has generally been believed that normal sleep and deep hypnotic trance are closely related states if not identical but until the advent of the EEG there was no reliable method of judging whether a person was asleep or not. In one patient the electroencephalogram (taken by Loomis) during the hypnotic trance was not basically different from the EEG taken during waking hours. To settle this question objective evidence obtained from more patients was necessary. Using a three channel Grass electroencephalograph with leads taken from the frontal, parietal and occipital regions, Dynes (1947) recorded the EEG tracings on five patients both during the waking state and during hypnotic trance. Anaesthesia to painful stimuli, complete amnesia for events which happened during the trance and the ability to carry out post-hypnotic suggestions were taken as the criteria for deep trance. Dynes found no essential difference between the tracings taken during the waking state and those taken either during the phase of induction of hypnosis or during fully established deep trance. The conclusion is drawn that there is no distinctive difference between the cortical activity (as recorded by the EEG) of a person in the normal waking state and that of the same person during deep hypnotic trance. These studies confirm the earlier findings of Loomis that normal sleep and hypnotic trance are of a different order.

CLINICO-PATHOLOGICAL STUDIES.

Lesions at the Cortical Level.—It has not always been possible to explain sleep disturbances in terms of lesions of specific areas of the brain. Although lesions of the hypothalamus due to neoplasm or to encephalitis lethargica are often accompanied by disorders of the sleep rhythm it is not easy to state that the hypothalamus alone is responsible for the control of sleep. The hypothalamus is connected with the thalamus, the basal ganglia, the mesencephalon and the brain stem. Neoplasms of the hypothalamus may also cause general disturbance of functions of adjacent structures either by compression or by obstruction of the cerebrospinal circulation.

Davison and Demuth (1945a) clinically observed 300 cases of sleep disturbances including insomnia, lethargy, somnolence, stupor, coma and unconscious states and studied fully 59 cases (57 in which autopsies were performed and two in which the diagnosis was verified at operation). Patients in deep coma who could not be aroused were not included. Their chief findings were as follows :

Location of lesion	Number
Cortical.	9
Cortico-diencephalic	25
Diencephalic	17
Mesencephalo-metencephalic	8

A solitary cortical lesion was found in nine cases and in none of these was there evidence of involvement of the hypothalamus. In two cases it was difficult to rule out compression of the hypothalamus but microscopically its nerve cells were found to be normal. Increased intracranial pressure was found in four cases only, indicating that such increased pressure probably plays only, a negligible if not totally insignificant role in causing sleep disturbances. One case had complained of diplopia. A boy, aged 13, had abnormal amount of hair, large genitals and large hands and feet. The remaining seven cases showed no ocular or endocrine changes. In one patient, aged 43, who complained of increasingly severe headaches, somnolence and weakness, craniotomy revealed two small meningiomas over the right frontal convolutions. Removal of these tumours was followed by disappearance of somnolence and the patient remained well for about five years after the operation.

From the study of this series of purely cortical lesions and from the cases reported by previous workers, Davison and Demuth are of the opinion that some fibres for the control of sleep may originate in the cerebral cortex, especially the hippocampal, cingular, frontal, premotor and temporal lobes. Lesions of these cortical areas or of the cortico-hypothalamic pathways may occasionally cause disturbances of sleep.

Lesions at the Cortico-diencephalic Level.—In 25 cases of sleep disturbances Davison and Demuth (1945b) found lesions in the cortico-diencephalic structures but in many instances it was not possible to decide whether somnolence was the result of a lesion of the cortex or of the diencephalon or of both. In 16 of these cases compression of the hypothalamus with pathological changes in its nerve cells was present. The hypothalamus was invaded in four other cases and partially destroyed in one case. In two cases it was merely compressed without

any microscopic changes in its cells and in yet another two cases there was neither compression of the hypothalamus nor changes in its cells. In 16 cases, in addition to compression or actual invasion of the hypothalamus there was also either compression or invasion of the basal ganglia with involvement of the strio-hypothalamic pathways.

Lesions at the Diencephalic Level.—The diencephalic lesions found in the 17 cases studied by Davison and Demuth (1946a) included adamantinoma, angioma, neuroblastoma, colloid tumour of the third ventricle, metastases from carcinoma of lung, meningioma, pituitary adenoma, glioblastoma multiforme, haemorrhage, encephalitis lethargica, paralysis agitans, tubercular basilar meningitis and torular meningitis. In 14 of these cases lesions were present inside the hypothalamus. Bilateral changes in the caudal part of the lateral hypothalamic area were found in 16 instances. In seven cases only the hypothalamus was involved without implication of the thalamus or the basal ganglia. Compression of the hypothalamus with degeneration of its nerve cells was present in three cases. In 10 cases the thalamus or the basal ganglia or both as well as the thalamo-hypothalamic and the strio-hypothalamic pathways were involved either by invasion compression or by oedema. In most cases the caudal part of the hypothalamus was chiefly involved but the anterior and middle parts were also affected in lesser degrees. In a solitary instance, the caudal part only was involved. It was therefore difficult to link up the insomnia or somnolence with the location of the lesion. The sleep disorders in this group included somnolence in 13 patients, reversal of sleep rhythm in two and insomnia followed by periods of drowsiness or stupor in two cases. In one of the patients who suffered from reversal of sleep rhythm a neuroblastoma was present in the most posterior part of the hypothalamus and the aqueduct of Sylvius. In four cases insomnia was followed by somnolence and as necropsy revealed lesions both in the rostral and in the caudal parts of the hypothalamus it was assumed that the former was probably involved first causing insomnia, and the latter was invaded next causing somnolence. Although from this study it would appear that somnolence may result from injury to the hypothalamus, especially the posterior part of the lateral hypothalamic area and its various pathways it would be difficult to exclude the role played by the thalamus or the basal ganglia in the causation of this symptom. Episodes of somnolence lasting 20 to 22 hours a day were present in a case reported by French (1947) in which a plasmacytoma of the hypothalamus was found.

Lesions of the hypothalamus do not invariably produce somnolence or even disturbances of sleep. In a case reported by Papez and Ecker (1947) there was no somnolence although the posterior part of the hypothalamus was found destroyed by an infundibuloma which had extended into the left thalamus. Fletcher and Bailey (1947) have recorded a case in which for nearly eight months there was neither somnolence nor sleep dysfunction until the onset of terminal coma which preceded his death. At necropsy the greater part of the hypothalamus was found replaced by a tumour extending laterally to the left internal capsule and also to the left temporal lobe.

In rats, incised wounds of the brain in one of several planes did not produce

any disturbances of sleep so long as the hypothalamus was left intact (Nautha 1946). When the incision was extended to the base of the brain leaving the opposite hypothalamus intact the sleep rhythm remained normal. In another set of experiments in which Nautha subjected the animals to bilateral section of the hypothalamus and unilateral section of the dorsal structures marked disturbances of sleep were noted in all the animals. Rats with bilateral lesions of the hypothalamus slept continuously so long as they were not roused by strong stimuli. When lesions did not extend ventrally beyond the central grey matter around the Sylvian aqueduct there was no interference with the waking capacity, suggesting the existence of a "waking centre" in the caudal part of the hypothalamus. From other experiments in which the rats suffered from sleeplessness it would appear that the function of sleep is regulated by a structure in the rostral part of the hypothalamus approximately conforming to the supra-chiasmatic and preoptic areas. Nautha believes that the lateral hypothalamic area containing the medial forebrain bundle is more responsible for regulating the sleep-wakefulness cycle than other areas.

Lesions at the Mesencephalo-metencephalic Level.—In the eight cases of sleep disturbances in which lesions were present in the mesencephalon and metencephalon Davison and Demuth (1946 b) found haemangioblastoma of the cerebellum in three cases, spongioblastoma polare, glioblastoma multiforme, meningeal fibroblastoma and metastatic carcinoma in each of the remaining cases. A man aged 36 had been drowsy and easily fatigued since the age of 24. He had complained of periods of sleepiness and weakness at the age of 12 and there was a recurrence of these spells 12 years later. At necropsy a haemangioblastoma of the cerebellum was found. The sleep disorders present in this group were as follows: spells of sleepiness in two, inversion of sleep rhythm in one, drowsiness followed by coma in one, lethargy in one, and somnolence in three cases. In all these cases the hypothalamus was normal. But the descending hypothalamic pathways and the nerve cells of the vegetative nervous system of the brain stem were affected in all instances. From this study it would appear that disturbances of sleep rhythm may result from lesions of the ascending and descending hypothalamic pathways of the mesencephalon (mammillary peduncle and mammillotegmental tract) and some of the vegetative nervous centres in the brain stem.

Anatomical Considerations.—The analysis of the clinico-pathological material studied by them enables Davison and Demuth (1946 c) to express their views on the centres and pathways concerned in the sleep mechanism. That this function is probably under some higher cortical control has been obvious from the ease and facility with which man can voluntarily fall asleep. Earlier work on sham rage has indicated that the cortex has some influence over the hypothalamus. It is reasonable to assume that some fibres for the control of sleep originate in cortical areas and are connected with the hypothalamus by means of cortico-hypothalamic pathways of which the main ones are as follows:

1. The medial forebrain bundle, part of the hippocampo-hypothalamic tract consisting of unmyelinated and myelinated fibres and which carry both ascending and descending fibres, runs between the

ventromedial olfactory correlation areas of the cortex and the hypothalamic areas.

2. The direct cortico-hypothalamic pathways such as those of the fornix (which contains cortico-hypothalamic, cortico-septal, and cortico-habenular fibres) and the inferior thalamic peduncle.
3. The indirect cortico-hypothalamic pathways are probably the fronto-tuberal tract and the neocortico-septal tract.

No hypothalamo-cortical connections have been demonstrated.

As sleep dysfunction was commoner in the group with cortico-diencephalic lesions it may be concluded that the cortex influences the main structure regulating sleep, namely the hypothalamus, either in an inhibitory or in an excitatory manner. Forced wakefulness and diurnal sleep being cortical functions it is obvious that the cortex is indispensable for the sleep-wakefulness cycle.

From the cases with diencephalic lesions it would appear that the hypothalamus is the main regulator of the sleep mechanism. Localisation on this material alone would be fallacious, as owing to the widely spread lesions, involvement of the areas adjacent to the hypothalamus either by compression or by oedema could not be ruled out. The hypothalamus is intimately connected with the thalamus, the striopallidum and the hypophysis by means of the thalamo-hypothalamic and hypothalamo-thalamic pathways, thalamo-mammillary fibres, mammillotegmental tract, stria terminalis, supraoptic commissure, hypothalamo-hypophysial pathways and the interhypothalamic pathways. Injury to the hypothalamus or to any of these afferent or efferent pathways may result in dysfunction of sleep. Damage to the hypothalamus which is a centre for wakefulness results in somnolence.

Some evidence, mostly clinical, exists that sleep mechanisms may be disturbed by lesions at the mesencephalo-metencephalic level. This part of the brain is connected with the hypothalamus by means of the (1) mammillary peduncle and the (2) mammillotegmental tract.

DISTURBANCES OF SLEEP.

Insomnia.—This word is here used in a very restricted sense to denote what would most appropriately be termed hypsomnia, and includes difficulties in falling asleep, disturbances during sleep and lack of sufficient sleep to maintain physical and mental health. During the war years in Great Britain and in many of the Central European countries the sleep of millions of human beings as well as of animals was disturbed nearly every night by the noise of planes, bombs or gun-fire. As judged by pre-war standards of sleep requirements very few beings enjoyed sufficient sleep for several years. Yet it is only a small minority of persons whose insomnia needed medical treatment, clearly suggesting that factors other than external noise were responsible for sleeplessness. The latter resulted from states of anxiety induced by psychological stress, difficulties of adaptation to new situations, separation anxiety, frustration, resentment, lack of faith and uncertainty as regards the final outcome, conflictual tension and so on. This was true both of the soldier and of the civilian. One of the lessons of the war years has been to emphasise, not

only that anxiety is the most frequent cause of insomnia, but also that disturbances of sleep and increased irritability are the two very earliest manifestations of an impending nervous breakdown.

Varying degrees of insomnia formed a common complaint of nearly every one in the theatre of war. This insomnia of the combatant soldier was also due to increased muscle tension caused partly by states of normal fear and partly by exposure to cold (Thompson 1946). In the experience of Grinker and Spiegel (1945) insomnia of varying degree, punctuated by vocal or physical actions, was almost the rule among combat crews. According to Kardiner and Spiegel (1947) inability to sleep was due to inability to relax, and inability to relax was due to the need for continuous vigilance—the negation of sleep. No soldier could relax among men whom he neither knew well nor trusted, and no soldier in the field could sleep so long as he experienced anxiety-laden battle dreams. Insomnia was the major symptom of “battle exhaustion” and was also the most predominant and persistent complaint of nearly every psychiatric casualty (Anderson, Jeffries and Pai, 1944, Kubie, 1944, Bartemeier, *et al.*, 1946, Pai, 1946 b).

Treatment of Acute Insomnia.—The psychological principles evolved in the treatment of insomnia in the soldier may be applied with beneficial results in the treatment of insomnia in the civilian. The ideal treatment is, of course, to remove the cause of anxiety or to remove the patient from the sources of worry. For the insomnia of the incipient stages of a nervous breakdown Rees (1945) recommends prophylactic sedation and points out how barbiturates have averted many a psychiatric casualty amongst soldiers in action and amongst civilians in bombed cities. Sedation for those who have broken down is valuable in preventing a conditioning to anxiety with consolidation of symptoms. Thompson (1946) on the other hand emphasises the importance of personal contact, reassurance and temporary relief from constant vigilance in combating the insomnia of the front-line soldier. Prevention and treatment are inseparable. Sedation is the start of real treatment, as it prevents the fixation of symptoms. For the combat soldier suffering from acute anxiety 24 to 36 hours of sleep is sufficient to remove the major symptoms. Even for severe cases with fitful nightmares, uncontrolled motor restlessness and excessive tremulousness Grinker and Spiegel (1945) advise only moderate sedation for 24 to 48 hours, as “deep narcosis” has not proved successful.

Evacuation plays a major part in the relief of insomnia (Anderson *et al.* 1944). To the “bomb happy”, the “battle saturated” and to the war weary soldier exhausted in body and in spirit the very word “evacuation” means a return to a world of sanity, love and peace. The simple human services associated with evacuation take on deep emotional and symbolic significance (Bartemeier *et al.* 1946) which it is impossible to over-estimate.

For the persistent insomnia of acute anxiety Pai (1946b) recommends medinal 10 gr. at 8 p.m. with a view to ensuring continuous sleep for about 10 to 12 hours daily. This method has the additional advantage that during waking hours the patient is enabled to take part in the social life of the hospital, which restores confidence and thus helps to reintegrate the cohesive forces of his personality.

Chronic Insomnia.—It cannot be too strongly emphasised that chronic insomnia may be a major and sometimes the only manifestation of recurrent and chronic anxiety. Disturbances of sleep which originally were precipitated by the conditions in the Forces, battle exhaustion, separation anxiety and so on may recur long after return to civilian life (Grinker 1946). Problems of resettlement and maladjustments to marital life are some of the commonest sources of worry. With each disappointment or minor frustration there may be a progressive loss of self confidence resulting, possibly, in a reactivation (Menninger 1946) or exacerbation of one or more of the symptoms of acute anxiety. Pearson and Cohen (1946) have described repeated catastrophic nightmares in ex-soldiers long after they had returned to their homes. In the opinion of Grinker the treatment of these civilians is likely to be the responsibility of psychiatrists for decades to come.

Insomnia of Depression.—Diaz-Guerrero *et al.* (1946) have studied the EEG patterns during sleep in six patients under the age of 40 who were suffering from depressive phases of manic-depressive psychosis. None had received either any previous sedatives or drastic therapy such as electric convulsions. When the EEG records of sleep were analysed they were found to vary within wide limits, owing to the variations in the actual duration of sleep. The average duration of sleep as indicated by the sleep pattern of the EEG was five hours and 42 minutes. The average period between retiring to bed and the onset of sleep was 41 minutes. When the EEG sleep patterns were compared with those of normal controls it was found that the patients had twice as much low voltage activity as the normal controls, i.e., 37.5 to 19 per cent. respectively. Wakefulness as judged by a return of the alpha-rhythm varied from 5 to 77 per cent. of the remainder of the night. Deep sleep as indicated by the appearance of spindles and random record varied from 6 to 41 per cent. of the night. When the EEG sleep patterns of the patients were compared with those of normal controls it was found that the percentage of low voltage records was twice as great for the patients as for the normals, i.e., the greater portion of the sleep of depressed patients was very light almost near to wakefulness. The percentage of spindles plus random records was smaller in the case of the patients, i.e., the period spent in deep sleep was much less than in the case of normal controls.

Rothenberg (1947) differentiates insomnia in a restricted meaning from general sleeplessness on the grounds that in the former the person is unaware of the deeper causes while in the latter the exciting cause is invariably anxiety. Unconscious death fantasies of long duration (as revealed by psychoanalysis) may result in insomnia. Its defensive character is indicated by the patient's inability to control this symptom by conscious will. Guilt feelings would appear to convert the death wish into a law of retaliation inflicting fear of punishment. Fodor (1945) points out that hidden behind the symptom of insomnia there may be claustrophobia, fear of death, fear of soiling bed sheets by masturbation and fear of this leading to insanity.

Sleep-walking and Sleep-activities.—So-called somnambulism is a state of dissociation occurring during apparent sleep, and characterised by general or local movements and by walking, of which the patient denies any knowledge

on waking up. It is obviously a manifestation of conflict between the super-ego and the id, or between duty and discipline on the one hand and self-preservation and pleasure on the other. Sandler (1945) reports somnambulism in 22 soldiers most of whom had presenting symptoms of neurosis. In four of the first 10 patients a history of sleep-walking in near relatives was obtained. In four other families some members were suffering from neurosis. A family history of either psychosis or suicide was given by three patients. In the majority of instances the somnambulist was found to be an immature and overdependent personality who was also heterosexually maladjusted. Tarachow (1945) describes the somnambulist act and discusses its probable meaning.

Pai (1946b) maintains that the features stated by earlier workers to be characteristic of somnambulism would seem really to be due to more than one condition. In his series of 117 patients whose presenting symptoms were sleep-walking and sleep activities, psychogenic causes were responsible for 97 cases, physiogenic conditions for 11 cases and hystero-malingering states for nine. Severe anxiety was the most frequent cause accounting for 89 cases. In acute cases there were other symptoms of anxiety which developed after exposure to intense enemy action. They all complained of lack of sleep and nightmares but had no knowledge of their nocturnal activities which consisted in jumping out of their beds and reliving their battle experiences. In patients suffering from chronic anxiety the walking was purposeless, movements slow and there were no tendencies to aggression. All but one had walked in their sleep prior to joining the army and sleep-walking was their pattern of reaction to stress. Patients suffering from hysterical dissociation were found to be very suggestible and responded to hypnotherapy. In two cases there was post-epileptic automatism of very brief duration. In nine cases sleep disturbances followed infections of the brain such as encephalitis and cerebrospinal fever (Pai 1944a, 1945, 1946a). Larceny, abnormal sexual practices, suspicions about marital fidelity and malingering were among the motives in the remaining patients who, during their nocturnal walks, were found to be fully awake. Schulte (1942) reports the case of a man who had walked in his sleep for several years and who used to make homosexual advances at night but had no knowledge of this on waking up. Schulte thinks the sexual perversion may be regarded as a sleep-walking equivalent. Pai (1946b) gives the differential diagnosis of the major symptoms in a table reproduced on p. 605.

Nightmares and Night Terrors.—Henderson and Gillespie (1944) still maintain that nightmares are distinct from night terrors and that the latter are almost confined to childhood. There does not appear to be any justification for this artificial distinction. Despert (1946) investigated 78 pre-school children—35 of whom were of the anxious type and 43 of the non-anxious type. Disturbances of sleep, especially both nightmares and night terrors, in addition to changes in respiration and pulse rate, were observed in children suffering from anxiety, fears and phobias. Kramer (1946) also points out that *pavor nocturnus* indicates a child's failure to cope with the problems of waking hours.

Both in children and in adults morbid anxiety appears to be the commonest cause of sleep disturbances, including nightmares, night terrors, talking and

DIFFERENTIAL DIAGNOSIS.

Diagnosis	Psychogenic causes				Physiogenic conditions		Hystero-malingering states
	Anxiety states		Hysterical dissociation	Epilepsy	Post-infective	Hystero-malingering states	
	(a) Acute Anxiety	(b) Chronic Anxiety					
Family history of	Neurosis	Neurosis	+ -	Epilepsy	-	-	
Neurotic traits in childhood ..	+	+++	+	-	-	-	
Sleep-walking in childhood ..	-	+++	-	-	-	-	
Obvious cause for anxiety ..	+++	+	-	-	-	-	
Dreams ..	++	+	-	-	-	-	
Talking or shouting ..	++	+	-	-	-	-	
Objective signs of sleep ..	-	-	-	++ +	-	-	
Duration of activities ..	10-15 min.	10-30 min.	Up to 2 hrs.	1-2 min.	Up to some hours	Some min.	
Motive ..	Pseudo-purposive	-	+	-	-	++ +	
Signs and symptoms during waking hours	Tremor ++ +	-	-	-	{ Residual signs of primary illness	-	
	Tachycardia +	+	-	-			
	Sweating ++ +	-	-	-			
EEG ..	-	-	-	Dysrhythmia	Abnormal	-	

walking during apparent sleep. Terrifying nightmares and night terrors were frequent among men who had been on a few operational flights (Grinker and Spiegel, 1945). They were also common among men exposed to battle stress (Pai 1946b, Kardiner and Spiegel 1947) and in others suffering from acute anxiety. These dreams and nightmares were characterised by visual hallucinations. As visual sensation has to traverse from the retina to the visual cortex—comparatively a much longer distance than that traversed by auditory sensation—it is not surprising that dreams consist mostly of visual hallucinations. A diminution in visual impressions before retiring to bed often results in a diminution or absence of dreams.

When London children were evacuated into the country the incidence of dreams and nightmares among them suddenly dropped to a low level. This was also the experience of children evacuated from other large cities into the country. Out of 405 children suffering from neurotic symptoms who attended clinics in evacuation areas in Northamptonshire only two were referred on account of sleep disturbances; at Reigate only two out of 190 children had sleep disturbances (Gillespie 1942). It would appear the visual cortex is over-stimulated in large towns with their cinemas, etc., leading to a higher incidence of dreams and nightmares.

Narcolepsy.—Electroencephalographic evidence in support of Kinnier Wilson's concept that narcolepsy is allied to the epilepsies has been offered by Cohn and Cruvant (1944) and by Roth (1946). A unique familial incidence was the outstanding feature of the series of 10 cases studied by Cohn and Cruvant. In each of five cases a family history of either narcolepsy or epilepsy was obtained. Each of two patients had one sibling who was narcoleptic and one who was epileptic. In eight out of 10 cases the EEG records taken between the narcoleptic attacks revealed abnormal wave forms usually seen in cases of grand mal and petit mal. In the early stages of the narcoleptic attacks the EEG records showed wave sequences similar to those observed during natural sleep. Cohn and Cruvant suggest that the narcoleptic syndrome should be called hypnolepsy, a term originally used by Foote. Roth (1946) reports a case with narcolepsy, cataplexy and sleep paralysis in which the EEG record was abnormal, containing paroxysmal discharges similar to those seen in cases of epilepsy. Roth believes that the emotional inhibition was probably responsible both for the diminished frequency of the cortical discharge and for the spike and wave pattern.

Fabing (1945) discusses the case of a soldier with narcolepsy, cataplexy and trance-like cataleptic attacks who went through the Tunisian and Sicilian campaigns. During the combat period he had repeated narcoleptic attacks, but surprisingly enough only two cataleptic attacks. This might be due to spontaneous remission (Dynes 1943) of cataleptic attacks. Fabing (1946) reviews the theories of the pathogenesis of the narcolepsy-cataplexy syndrome and advances a theory which is essentially an elaboration of the formulation of Kinnier Wilson. He thinks it is not the quality but the magnitude of the emotional stimulus which causes the cataleptic attack. An ultramaximal stimulus so disorganises the activity of the cortical cells that the abnormal stimulus instead of causing excessive excitation actually causes inhibition—

(the ultraparadoxical phase of Pavlov). Not many clinicians would agree with this view, as in the vast majority of cases the cataplectic attacks are precipitated by simple excitement or laughter, which can hardly be called ultramaximal stimuli. According to Fabing, summation of repeated stimuli, by producing the ultraparadoxical phase, results in widespread inhibition of the cortical centres, leading to the motor and psychic phenomena of sleep as seen in the narcoleptic attack.

Magnussen (1943) has continued his studies on the relation between peripheral vasodilatation and "vegetative preparedness" for sleep. In three narcoleptics the skin temperatures studied included those taken on the rapidly reacting pulp of the toe as well as on the dorsal surface of the foot. By means of an automatic device the thermoelectrical measurements were recorded photographically for periods of up to 72 hours. A rise in the skin temperature was evidence of vasodilatation and corresponded either with a sleeping period or signified the autonomic preparations for sleep during daytime. From these records it would appear that vegetative preparedness for sleep forms presumably the basis of the narcoleptic attack. Despite the numerous errors in these experiments Magnussen advances a hypothesis based partly on these experiments and partly on the earlier findings of Ranson and of Bremer. According to this hypothesis the waking centre of the hypothalamus which is partly influenced by peripheral stimuli also possesses a certain degree of automatism. Diminished activity of this centre indicating a decrease in sympathetic activity results in the condition of vegetative sleep preparedness which facilitates the onset of sleep.

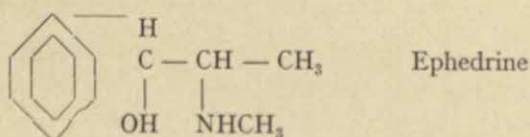
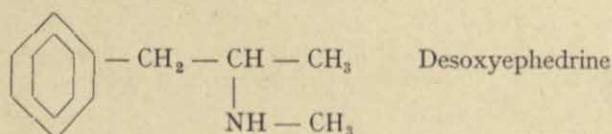
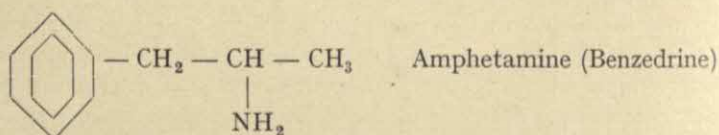
Hypoglycaemia and Narcolepsy.—Hypoglycaemia plays only a minor role in the aetiology of narcolepsy, but occasionally cases are reported (Marinesco) in which administration of sugar causes rapid awakening. In a patient of Delay (1942) the attacks of narcolepsy and cataplexy of ten years' duration were found to be due to low blood sugar. Administration of sugar afforded immediate relief, thus establishing that narcolepsy may be one of the rare nervous manifestations associated with hypoglycaemia. To distinguish this condition from other forms of narcolepsy the term "pancreatic encephalosis" has been suggested. The relation between hypoglycaemia and narcolepsy is rather obscure in the case discussed by Riser and Dardenne (1946). The patient who suffered from attacks of irresistible sleep, sometimes lasting for 20 to 24 hours had also symptoms of endocrine dysfunction such as obesity, amenorrhoea, polydipsia, polyuria and so on. The blood-sugar level was very low, but induced hypoglycaemia produced only slight increase in somnolence without narcoleptic attacks. Administration of pituitary extract relieved the polydipsia and polyuria but not the narcolepsy. Administration of sugar only very slightly improved the somnolence. Marked improvement, however, followed six therapeutic electric convulsions, although during menstrual periods there was a tendency to somnolence. These results have been attributed to the action of the E.C.T. on the hypothalamus or its connections.

Schizophrenia and Narcolepsy.—Lehrman and Weiss (1943) have described a case of paranoid schizophrenia who suffered from narcolepsy-cataplexy syndrome for 14 years. Her psychosis, with auditory and visual hallucinations

and ideas of reference, began six months prior to her admission to hospital. Her paranoid projections seemed to originate in her concern over her attacks of narcolepsy, but when the latter were controlled by benzedrine the diffuse paranoid ideas persisted in a general way.

Psychogenic Narcolepsy.—There is no doubt that in many instances narcolepsy may be a psychogenic symptom. In a case reported by Spiegel and Oberndorf (1946) the symptoms included periods of diurnal drowsiness, attacks of narcolepsy and cataplexy, episodes of prolonged sleep lasting up to 36 hours, hypnagogic hallucinations and polydipsia. There were also hysterical conversion symptoms and attacks of vomiting which alternated with excessive thirst. Discussion of certain distressing topics seemed to cause emotional excitement and exacerbation of symptoms followed by drowsiness. It was obvious that the narcoleptic attacks were associated with the patient's psychosexual history and incestuous practices. Prolonged cathartic treatment resulted in substantial improvement. With the disappearance of the narcoleptic attacks a conscious feeling of guilt was experienced. Psychogenic narcolepsy is an unconscious method of satisfying forbidden desires without consciously experiencing guilt feelings. It may also imply punishment for these unhealthy desires. Schulte (1942) describes a narcoleptic who always led a normal sexual life but showed temporary homosexual tendencies while under the influence of alcohol.

Treatment of Narcolepsy.—Eaton (1943) reports the results of administering desoxyephedrine, which has a chemical structure similar to amphetamine and ephedrine, to 15 out-patients whose presenting symptoms were those of narcolepsy although 10 had cataplexy as well. Some had been previously treated with amphetamine and others were given a trial period with this drug so that all could compare the effects of the two drugs. Two or even three tablets



were to be taken if one tablet of 2.5 mg. of desoxyephedrine did not give the desired result. Twelve patients found desoxyephedrine more effective even after periods ranging from seven to 16 months. Two discontinued it after a week as they preferred amphetamine. None complained of untoward reactions.

Roskam (1946) gave Revoxyl (dibenzylmethylamine) to two patients, one of whom benefited by its use but the other did not.

Cataplexy and family periodic paralysis have some common features and as the latter condition is now considered to be due to faulty potassium metabolism it is reasonable to suspect a similar disturbance in the former. Dynes (1943) treated six patients suffering from severe and persistent cataplexy with potassium chloride. In some cases administration of potassium chloride 30 grs. daily brought about moderate improvement. Others responded favourably to increased doses up to 75 grs. daily. Cataplectic attacks were not totally eliminated in every case. To patients who received only potassium chloride it was found necessary to give also benzedrine to control narcolepsy. There was no evidence of faulty metabolism nor was clinical improvement followed by any change in serum potassium.

Experimental Narcolepsy.—An interesting contribution is that of Carrega Casaffousth and Brage (1946) who describe a reaction which they observed in 10 epileptic patients when carbogene was injected intraspinally for diagnostic or therapeutic reasons. In all the 10 cases intraspinal injection of 60 to 150 cc.m of carbogene was followed by cataplexy lasting about three minutes. In two patients narcoleptic attacks were also observed.

Sleep Paralysis.—In the two cases of sleep paralysis reported by Rushton (1944) the EEG was normal and there were no narcoleptic attacks.

Brill and Farrell (1946) have described two cases of pseudo-narcoleptic syndrome in soldiers who were found to be malingerers.

Sleep and Migraine.—Gans (1943) discusses the interrelation of sleep and migraine. He found that many of his migrainous patients had described their sleep as "very heavy and deep" and this in the opinion of Gans was probably the cause of the migraine. He obtained good results by reducing the duration and depth of sleep!

Hypnagogic Hallucinations.—After long self-observation during the process of falling asleep Rouquès (1946) claims to have seen clear and perfectly realistic images of objects and of human figures of normal size. Attempts to obliterate these visions by deliberately imagining other objects were not successful. After a day's fishing there was often a vision of slowly flowing water.

Hypersomnia.—Pathological sleep may be either paroxysmal, periodic or prolonged. Periodic and episodic states of sleep became known from the Frankfurt Clinic and are often associated with the names of Kleist, Kleine, Lichenstein and Stadler. Since then a few cases have been reported in which in addition to periodic somnolence there have been one or more common symptoms of unknown aetiology.

Periodic Somnolence and Morbid Hunger.—The Kleine-Levin syndrome consists of periodic attacks of sleepiness lasting several days or weeks, abnormal hunger, motor unrest and mental symptoms of mild confusion, irritability, incoherent speech and occasionally hallucinations. Critchley and Hoffman (1942) report two cases of this syndrome in which the glucose tolerance and insulin-tolerance tests were within normal limits. The EEG in one case showed on vigorous overbreathing a large intermittent delta discharge involving both frontal lobes suggesting dysrhythmia but there was no conclusive evidence

that a frontal lobe lesion was responsible. The authors admit that they were unfortunate in not seeing the patients during their actual attacks. Neither the patients' subsequent progress in hospital nor the results of follow-up after discharge from hospital have been reported. Two more cases have been published by Ronald (1946) but the case histories are again incomplete and their subsequent fate has not been reported although both the patients were living not very far from the hospital.

To account for such a variety of symptoms on an organic basis it would be necessary to postulate multiple lesions scattered widely in the central nervous system. Patients with such organic lesions are unlikely to survive more than a few weeks. The two predominant symptoms in this syndrome are somnolence and hunger. Other symptoms appear to be secondary and are of minor importance. Patients suffering from such symptoms have been seen at large neurosis centres like Mill Hill Emergency Hospital and have been diagnosed as cases of hysteria and treated successfully.

Periodic Hypersomnia During Menstruation.—Lhermitte (1942) discusses the case of a girl who during her menstrual periods would fall into a deep sleep lasting four to five days. When awakened at meal time by strong stimulation she would demand food and devour everything that was offered. At other times her appetite was normal. There were no positive findings and X-ray of skull was normal. In view of the scantiness of her menstrual flow she was given injections of gonadotropic hormone and ephedrine, which relieved her of the attacks of hypersomnia. Lhermitte expresses the view that some diencephalic syndromes occur rhythmically and very regularly with menstruation, so that these syndromes may be caused by a hormonal influence on a previously sensitized diencephalic vegetative system. Lhermitte, Hécaen and Bineau (1943) studied another case of prolonged hypersomnia during menstruation. Each attack was preceded by severe headache and vomiting. The sleep which was at first light began gradually to become longer and deeper, and hypersomnia occurred apart from menstruation. No other symptoms were present and radiography of the skull showed no abnormalities. Clinically moderate mental deficiency, inequality of the tendon reflexes and an extensor plantar response were found.

Grosch (1943) presents seven cases in which the attacks of sleep occurred regularly at four-weekly intervals. There was a strong family history of epilepsy or epileptoid conditions in the majority of these cases. Based partly on this material and partly on the earlier publications from the Frankfurt Clinic, Grosch concludes that these attacks of periodic sleep which occur almost exclusively in men are really epileptoid states. Only one case was seen in a woman, in whom the first attack of sleep occurred during the climacteric, whereas the males were all attacked at puberty at a time of excessive growth.

Brachialgia Statica Paraesthetica.—According to Wartenburg (1944) this condition which occurs between the ages of 40 to 45 is characterised by transient pain and paraesthesia in the area innervated by the ulnar nerve of the "arm upon which the patient is not lying." Signs of organic lesions are absent and X-ray findings usually negative.

DISCUSSIONS ON SLEEP.

L. Hess (1943) points out that although there are obvious signs differentiating physiological from pathological sleep, the concept of a sleep-regulating centre could be applied to some of the conditions of pathological sleep. In uraemic patients, for instance, the miosis, ptalism, the vomiting and diarrhoea might be due to irritation of *one* centre in the diencephalon not far from Economo's centre. The inhibition arises in the midbrain similar to that which results in natural sleep. In pathological conditions the common findings are oedema of the brain and clinically, except in morphia poisoning, normal pupils, and absence of Bell's position of the eye balls. W. R. Hess (1943) still maintains that sleep is an active process produced by stimulation in the hypothalamic area, but from his views as regards the "dynamogenous" hypothalamus it is difficult to draw any conclusions of practical importance. As a result of hypothalamic stimulation some of his cats became drowsy and inactive (Hess 1944) but did not fall asleep. Hess has given the name "hypothalamic adynamia" to this state of drowsiness with the characteristic plasticity of the animals to distinguish it from the typical sleeping state. In reviewing his results Hess (1945) reiterates his opinion that sleep may result from stimulation of some area in the central nervous system.

The hypothesis that one of the functions of sleep might be to set in motion the circulation of the cerebro-spinal fluid in the cerebrum has been advanced by Gans (1946). Levin (1946) recalls that "delay" is one of the four methods used by Pavlov for inhibiting conditioned reflexes. It is the interval between the time of application of the conditioned stimulus and the moment of reinforcement. When a person who has been expecting to carry out a certain task is compelled to wait until his turn arrives the process of restraining his impulses may result in sleepiness. The inhibitions would appear to have over-shot the mark and irradiated widely resulting in natural sleep. Myerson (1947) expresses the view that depressive states are dependent on disturbances of the sleep-wakefulness cycle and the insomnia of depression is called "dyssomnia."

Psychoanalytic Contributions.—In a bioanalytical contribution to the problem of sleep and wakefulness Jekels (1945) points out how closely ideas of sleep and death are associated in people's imagination. He emphasises the fact that the loss of ego feeling in the process of falling asleep is experienced as *dying*. The onset of sleep involves an active dynamic process—that of withdrawal from the world. Sleep is invariably accompanied by dreams and it is the function of dreams to provoke awakening. Jekels supports Claparède's biological theory of sleep according to which sleep is an instinct.

Lewin (1946) introduces a new term "the dream screen" to denote the background against which dream images appear. According to psychoanalytic theory the dream screen represents the breast and material from the *pre-conscious* and *unconscious* which threatens to disturb sleep appears disguised as dream images. The dream screen may also represent the wish to sleep. A dream without images, i.e., only the blank dream screen may occur and this represents primary infantile sleep. From the dream analysis of a schizophrenic patient Lewin obtained material in confirmation of his theory that blank dreams do occur. This patient's erotomanic delusions corresponded to the images missing

from the dream screen. Owing to the identification of ideas of eating and of being eaten the wish to sleep implies a wish to be eaten up. On account of the fusion of the breast and of the sleeper's skin some cutaneous qualities may also be implied in the dream screen.

As sleep fulfils a protective function against physical and mental exhaustion, from the analytic viewpoint it may be described as a nightly regression associated with a temporary denial of reality (Davison and Demuth 1946c). Sleep and its disorders may assume the role of a defence mechanism against harmful conflicts resulting from the innate instincts on the one hand and the demands of society on the other. In cases of psychogenic disorders sleep or its dysfunction assumes the character of a retreat either to dodge hostile reality or to obtain some gratification.

MEDICO-LEGAL STUDIES.

Somnambulism and Criminal Responsibility.—Doctors may be called upon to give evidence as to the state of mind of an accused person at the time of an alleged somnambulist act. From his study of 117 patients Pai (1946b) expresses the view that post-epileptic automatism is the only condition in which a person may be said to be asleep. A person who commits a crime during this phase must be considered to be without a *mens rea*. In all other cases of so-called sleep activities the performer may be considered to be awake, although the extent and degree of awareness may vary within wide limits. The type and nature of the activities indicate the degree of consciousness at the time. Complicated and goal-directed actions which require considerable skill, co-ordination and judgment cannot be carried out without recalling old associations of ideas and without being clearly orientated as regards time, place and situation. As such actions would be evidence that all the higher psychic processes associated with full consciousness are functioning efficiently it would be difficult to sustain a plea of irresponsibility.

A sensational Old Bailey trial (R. v Mathieson 1946) was that of a sailor who pleaded "not guilty" to murdering a married woman. The defence put forward the view that at the time of the alleged murder the condition of the accused was analogous to that of a sleep-walker. The jury returned a verdict of guilty and the judge sentenced him accordingly. After the man was hanged one of the newspapers revealed an account of his life describing him as a "thief, man-about-town, and it is almost certain, double-murderer" who was known in the London underworld as a cunning railway thief and so on, which left no doubt as to the state of his mind at the time of the murder.

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PSYCHOTHERAPY.

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THE number of books and papers on the various branches of psychiatry produced in the last few years has been so large that no reader, however assiduous, could hope to assimilate all of them. In consequence a demand has arisen for epitomes of the literature. This demand has been met by the publication—monthly, quarterly and annually—of journals and books containing abstracts and critical surveys. Contributions on psychotherapy are counted by the hundred and there have been innumerable allusions to psychotherapy in papers devoted to other subjects. Those who require a complete survey of recent literature on psychotherapy should consult the volumes just mentioned. The scope of these may be judged by one example: the 1948 edition of *Progress in Neurology and Psychiatry* contained reviews of more than 2,800 papers.

The aim of this article is more limited. Reference will be made to developments in psychotherapy and the principles upon which these are based; the use of art in therapy; physical methods in conjunction with psychotherapy; the application of psychotherapy in certain disabilities; and group therapy.

I.

Snyder (1947) discusses the areas of agreement in therapies and the evolution of different techniques in a review of contributions on psychotherapy, psychoanalysis, brief psychoanalysis, hypnotherapy, psychodrama, narcosynthesis and group therapy. The main trends regarded as noteworthy are the attempt to modify or vary the early techniques, the unifying of psychotherapeutic approaches, the use of briefer therapy and of group therapy. The hope is expressed that psychotherapy, long an art, is in the early stages of becoming a science. Towards this end reference is made to the experimental use of the phonographically recorded interview. The use of such records is not of course new. But it is conceivable that this procedure will play a part in reaching a measure of agreement upon psychodynamics, and so be a guide to the therapist in treatment and in assessing the type of patient who will respond to treatment. Agreement upon the dynamics, the force or forces within the psyche, would naturally have considerable effects on therapy. Alexander and French (1946) and their colleagues at the Chicago Institute of Psychoanalysis have reached conclusions on this matter after seven years of research. Following Ferenczi and Rank, the authors hold that emotional experiences in the transference (rather than intellectual reconstruction of the past) provide the therapeutically dynamic—and therefore valuable—material. They do not

believe that the transference is a mere reproduction of early experiences, because the attitude of the analyst is by no means the same as that of the parents and others who originally evoked the reactions of the patient. In treatment, therefore, attention is focussed upon the dynamics of each patient and therapy adjusted accordingly.

Considerable attention is paid to the planning of treatment. The practice of treating all patients in the same way is disputed. Therapeutic methods should be adapted to individual needs. What is described as the almost superstitious belief of some psychoanalysts that quick therapeutic results cannot be genuine is not accepted. Neither is the belief that the prolongation of an analysis is justified on the grounds that the patient's resistance will *eventually* be overcome and the desired therapeutic results achieved. The authors, like many other therapists, were puzzled by the baffling discrepancy between the length and intensity of an analysis and the degree of therapeutic success. This accounts for the introduction of a flexible form of analysis to replace the traditional form. The daily visit is no longer obligatory and often interviews are given at considerable intervals. The actual life situation of the patient is used to reinforce the therapeutic experience of analysis. The analyst gives advice on the conduct of current events in the patient's life. The claim is made that this is psychoanalysis refined and moulded, so that it can accomplish specific purposes more efficiently and in less time.

The authors point out that Jung and others have made contributions to psychodynamic theory and psychotherapeutic technique based on psychodynamic principles. For lack of space these contributions are not discussed. This is a pity. Many features in the "flexible" approach have been current practice for many years amongst analysts whose work is based on the views of Jung. An example is the emphasis laid by these authors on the importance of the present day problem: "The more we keep our attention focussed upon the patient's immediate problem in life, the more clearly do we come to realize the patient's neurosis is an unsuccessful attempt to solve a problem in the present by means of behaviour patterns that failed to solve it in the past."

Fromm-Reichmann (1943), while using psychoanalytic principles, also advocates less rigidity in the technique of treatment. Only those who find it a help should "lie on the couch in the classical manner." Some patients prefer to have the analyst in sight, and there is no objection to this. Freud, we are told, could not bear to have patients gazing at him for eight hours of the working day!

Oberndorf (1946) is also amongst those who recognize development and change in the theory and practice of psychoanalysis. The emphasis has shifted from infantile trauma and genital zones to the present enthusiasm for repressed aggression as the fountain head of all somatic conversions. The clinical effectiveness of the therapist, we learn, depends upon his skill in timing his comments as well as upon their accuracy and appropriateness. Should the physician be active or passive? Oberndorf sees much in favour of activity. This leads to fewer and well-spaced interviews. The word suggestion is practically obsolete in psychoanalytic literature. But this writer believes that the entire procedure of psychoanalysis has a suggestive implication and that the

analyst is influenced by it. Hence the wide disparity of thought on critical matters amongst experienced psychoanalysts; each shifts the emphasis to those aspects of psychoanalytic theory which best meet his subjective clinical talents.

Rioch (1943) recalls Freud's ready admission that the results of psychotherapy rest upon a basis of suggestion through and by means of the transference. He discusses critically the events of transference and in particular the correlation between hypnotism and the transference phenomena in psychoanalysis. There is no such thing as an impersonal analyst. Whether conscious of it or not, the analyst does express, day in and day out, overt evidence of his own personality in relationship to the patient. Analysis thus tends to create, in the patient, "a sense of being under a sort of hypnotic spell." Failure to recognize and to resolve this, makes the analysis unduly prolonged and limits its efficacy.

Leahy (1948), unlike Oberndorf and Rioch, writes with unwavering conviction—what an asset to the therapist!—of the value of treatment by suggestion. He is concerned only with the clinical application of suggestion and not at all with its limitations. The theme of his book is the conquest of fear. The technique of suggestive therapy is fully explained. While no claims are made that suggestion is infallible, it is constantly successful in the removal of morbid fear. Rioch's observation that there are no impersonal therapists would certainly not be disputed by Leahy.

Horney (1942) is another who believes that the dynamics of the psyche can be dealt with by means outside "classical" psychoanalysis. While holding that psychoanalysis will remain a method of therapy for specific neuroses, she observes that many patients, not suffering from neurosis, turn to psychiatrists for help because they cannot cope adequately with life and its relationships owing to some hidden element in their personality. Every analyst relies upon the unconscious mental activity of his patient. This underground activity comes to light not only in the analytic session, but in the interval between sessions; and the recognition of this enables the patient to share in the work of analysis in a constructive manner. The patient who has cultivated self-recognition and learnt something of mental dynamics, may pursue a method of self-analysis without the aid of an analyst. This is particularly useful in a character disorder. Self-analysis is distinguished from mere introspection and from orthodox analysis. The patient has a unique relationship to himself. If he can learn a method of overcoming resistance to self-observation, he has all the material at his disposal for self-analysis. Self-analysis is framed on the background of psychoanalysis. But the method of handling the transference is by no means clear.

The most notable development in psychoanalysis in recent years is associated with the name of Melanie Klein. In Great Britain, indeed, the adjective *Kleinian* often replaces *Freudian*. The theoretical and therapeutic aspects of Klein's concepts go together and so it is impossible to describe therapy without discussing psychopathology. It is therefore beyond the scope of this article to specify the distinctiveness of therapy entailed by these new views. Appreciation of Klein's work, in so far as it relates to psychotherapy, can only be reached by a study of the special literature as a whole. A paper by Klein,

published in 1935, upon the psychogenesis of manic-depressive states, altered (for many workers) the clinical approach to depressive illness in children and adults; and had a marked effect on psychoanalytical therapy in general. Furthermore, progress in the therapy of adult and child patients came about with the understanding of early infantile paranoid and schizoid anxieties and mechanisms and of the early stages of ego development. The 1935 paper and others on the same theme have been included in a larger work by Klein (1948). Mrs. Klein has kindly referred the writer to various papers and they indicate the influence her observations have had. These include articles by Riviere (1936), Isaacs (1940), Heimann (1942), Milner (1944), Fairbairn (1941 and 1944), Winnicott (1945), Klein (1946), and Scott (1948).

Klein believes that from the beginning of life libido is fused with aggressiveness, and that the development of the libido is at every stage vitally affected by anxiety derived from aggressiveness. Much of this early development is unconscious, and to reveal it considerable use is made of drawings in the analysis of children. Klein discusses super-ego development in an account of the treatment of a child (Rita). The appearance of the super-ego was traced "definitely to the beginning of her second year." But other experiences led Klein to conclude that "the beginning of Rita's super-ego reached back to the first few months of life."

Glover (1945) presumably had statements similar to this in mind in his criticism of Klein's description of mental development as "purely hypothetical reconstruction." In the Klein system of child psychology he sees the first sign of clinical specialization in psychoanalysis. This was followed by a clinically unjustified acquisition of prestige on the part of child analysts. To this prestige factor Glover attributes some of the chaos that has recently arisen in psychoanalytic circles in Britain. He contends that even if Klein's entire system were sound, i.e. if infants a few months after birth possessed a psychic apparatus already differentiated into ego and super-ego, capable of the elaborate and sophisticated system of unconscious and preconscious fantasy Klein describes and, *a priori*, capable of developing a classical transference neurosis, this would still not justify the assumption of a possible "analytic situation." Neither the transference nor its associated resistances could be analysed until their meaning could be conveyed.

The assumptions made by Klein about early infancy (the first two years of life) cannot, says Glover, be confirmed by direct analysis, whereas conclusions drawn about the unconscious content of five-year-old children from the analysis of adults can be confirmed by actual analysis of five-year-olds. The Klein system has broken through the limitations of metapsychology to postulate a bio-religious system which depends on faith rather than on science.

In a later essay, Glover (1948) gives an account of Freudian principles "drawn from the writings of Freud and from those of his followers who have applied these principles without deviation." In his view "some recent theories of child psychology which have gained currency amongst a small group of psychoanalysts in this country, constitute a deviation from Freudian principles and practice, combining some of the errors of both Rank and Jung."

Domarus (1948), from a study of several polyandrous societies, shows that there are ways of solving the Oedipus complex and related complexes, very different from those with which most therapists are familiar. He points out that psychotherapy, particularly psychoanalysis, proceeds from a number of assumptions largely derived from the understanding of man's early environment—the family.

If it be accepted that our societal set-up causes psychoneurotic diseases and that psychoneurotic conditions cause psychosomatic diseases, then a different societal set-up should produce different psychoneurotic conditions or none; and these again should cause different psychosomatic diseases or none.

Autopsies and observations on the Japanese Ikinawans and on the inhabitants of Guam Island have been published. The former are comparatively free from psychoneurosis and psychosomatic diseases, while the latter group, who have been influenced by American habits and customs, suffer from both. The author argues that if psychotherapy is to succeed, that is, if the patient is to become adjusted to the requirements of a society, extensive changes in sociomental attitudes are necessary. How these changes are to be brought about is another matter. Nevertheless, this contribution is a reminder that opinions on what constitutes a "good society" may need revision.

Gerhard Adler (1948) assembles in book form a collection of lectures on Analytical Psychology. The lectures have been enlarged and revised so that the book provides an adequate account of the theory and practice of psychotherapy based on Jungian concepts. A comparative study of analytical psychology, psychoanalysis and other types of analysis, shows the distinctive features of the Jungian approach. The book is illustrated with numerous drawings by patients and so serves as an introduction to the use of such material in dream analysis. Attention is also given to religion, which, like psychology, is concerned with ways of life and is thus linked with mental and spiritual health. Religion is treated as a phenomenon of the psyche, and as such is an appropriate subject for psychological enquiry.

Layard (1942) records in detail the participation of therapist and patient in an analysis conducted almost entirely upon the content of dreams. It is claimed that this has not been done previously. A theoretical discussion of the analytical procedure is followed by a disquisition upon the mythology of the hare—an archetypal figure prominent in certain of the dreams.

Berg (1946) in the clinical study of one patient, also describes the part played by analyst and analysand. A verbatim report is given of their respective contributions at all critical points in the analysis. A later volume by Berg (1948) deals more fully with the implications of treatment by psychoanalysis. He prefers (as did Freud) not to be limited by the confines of past discoveries and regrets what he considers to be the extreme conservatism of the majority of Freud's followers.

The extensive use of dreams in psychotherapy, mentioned above in referring to the books by Gerhard Adler and Layard, may be contrasted with their use in Individual Psychology. Alexandra Adler (1948), following the teaching of her father, Alfred Adler, regards the dream as an illusory picture of how to succeed in disregard to the logic of the situation. Courageous persons, she

believes, do not dream. This derogation of the dream is not, however, substantiated. Alfred Adler once stated in a public lecture in London that he had not had a dream for sixteen years—a remark not, of course, mentioned in this volume. The book is mainly concerned with the neuroses of childhood and post-traumatic neuroses.

Mueller and Kaney (1947) have developed "a technique of acceleration" in the treatment of a selected group of patients with conversion hysteria. An eclectic use was made of the Freudian and Adlerian approaches with the younger, and of the Jungian concepts with those in middle life. "Personality study as a psychobiological therapy" was used rather than free-association, which was thought to be too slow. While psychoanalytic principles were employed, psychoanalysis was impracticable "for the same reasons that it is so often impracticable." A distinctive feature is the co-operation between the therapist (described as a psychoanalyst) and the psychiatric social worker. Narcosynthesis, hypnotherapy, active analysis and case-work therapy were all applied to secure a therapeutically effective discharge of emotion with a recall of repressed memory.

Stengel (1948) points out that obsessional symptoms and depression often co-exist and that when depression occurs on a background of obsessional neurosis the pathological mechanisms are modified. Regression, leading to a complete break with reality, is counteracted. The aggressive impulses which in the typical depression are mainly directed against the self are diverted against external objects. Thus the obsessional neurosis will be clearer and less unexpected if symptoms of depression as well as obsessional features are kept in mind in treatment and in case-taking. It is important to recognize what we are trying to cure.

Brenman and Gill (1947) provide a survey of the therapeutic applications of hypnosis. In addition they evaluate the manifold attempts to rationalize these systematically and so link the therapy with the presumed aetiology of the illness. Chapters are devoted to the history of hypnosis, methods used to induce hypnosis, the factors in hypnotic susceptibility and types of hypnotherapy. Current theoretical systematizations are considered to be inadequate and consequently the time has come to estimate their value in relationship to the work of Freud. A series of case studies and an experimental study of hypnotic techniques in tension states form the background of this work.

Stengel (1943), in a study of patients with pathological wandering, concludes that the hysterical mechanisms in fugue states are only part of a complex aetiological picture. Consequently, the therapist in considering the treatment of a "fugue" state should use the term in an exact sense. The tendency to call transient states of altered consciousness fugues, irrespective of the behaviour of the patient, has produced unsatisfactory results. Hysterical and epileptic wandering states (Stengel does not differentiate between these), psychopathic, schizophrenic, general paralytic and even neoplastic fugues with the impulse to wander, show very different clinical pictures. Although Stengel makes only passing references to psychotherapy in this article his observations are important when psychotherapy is contemplated.

Parfitt and Carlyle Gall (1944) formed the impression that the incidence

of psychogenic amnesia, so common during the second world war, was on the increase before the war. The use of the term psychogenic amnesia is supported by positive evidence of a psychogenic process consistent with such a diagnosis and the exclusion of other causes. Two-thirds of the patients had fugues, but, unfortunately, few details of the fugues are given. The authors had "almost uniform success in getting patients to face their memories by simple persuasion." Narcosis and hypnosis were rarely required and had nothing to recommend them. The significance of narcosis, they believe, lies in the suggestive effect of the injection, the paraphernalia required and the feeling experienced as the drug begins to take effect. While other therapists have had different experiences with narcosis, it is too often employed by psychiatrists who lack confidence in their capacity to use purely psychological methods.

Rümke (1948) enumerates non-psychogenic agents responsible for neurosis and considers that psychogenesis has been over-estimated. This limitation should not lead to psychotherapeutic nihilism. By psychotherapy alone can the patient be brought to social adaptation. The reduced importance of psychogenesis will, however, make us more modest in our anticipations.

Schneck (1946) values bibliotherapy as an adjuvant in psychotherapy. A judicious choice of books activates personal problems, illuminates the significance of family relationships and enables interviews to proceed constructively and rapidly. Gottschalk (1948) also noted a saving of time by providing reading prescriptions. While many therapists suggest books to their patients, they might hesitate to adopt a technique of bibliotherapy which could hinder the release of unapprehended emotion and evoke resistances.

Jung (1946) has subjected the phenomena of transference to an extensive investigation. When prolonged therapy is called for, treatment always centres round the phenomena of transference. Yet despite its importance it is not always necessary for cure. Transference cannot be insisted upon. When it is slight, other therapeutic factors are used. Nevertheless, transference is a critical phenomenon whose occurrence is as significant as its non-occurrence.

The therapist, by accepting the patient's difficulties with understanding, exposes himself to the disquieting contents of the unconscious and their inductive effect. The activated unconscious of the patient is projected upon the analyst and constellates his unconscious material. There is thus an inevitable relationship of mutual unconsciousness. Awareness of this psychical infection brings about the right attitude towards the patient. The clinical relationship is compared to the alchemistic concept of *conjunctio*—what we now call "chemical compound." The therapist will be inclined to place the onus on the patient. Yet he must feel that he, too, is committed. The activation of the unconscious is the critical factor. Many problems need more than intelligence and sympathy and make demands on the whole personality—"the art requires the whole man."

The clinical phenomena of transference are not described in this volume, as Jung is writing exclusively for therapists with considerable experience.

Federn (1943) has contributed three papers on the "Psychoanalysis of Psychoses." The method sponsored is said to be true psychoanalysis, i.e. the acceptance of Freud's own definition of his method, and not psychotherapy

of another kind with psychoanalytical knowledge as a partial basis. Nowadays it is accepted that a transference can be established and that an analysis is possible in patients with narcissistic mental disease. But the transference is unstable and does not warrant use of the psychoanalytical method employed with neuroses. The main difference arises with resistance and transference. In psychotics the resistances are already broken and have to be re-established by psychoanalysis; and "re-repression" must be created. The couch is not used; the "basic" rule (free-association) is not imposed; the analyst is in constant touch with the relatives; and success is dependent on favourable external circumstances. Federn used a woman helper who was called in towards the end of the session. She, indeed, shared the transference, for the psychotic depends more on reality than the neurotic and becomes perturbed if forced to transfer his mother-relationship to a man. These papers deserve the consideration of therapists who work with psychotic patients.

Barbara (1944) also disagrees with the view that a positive transference is impossible in the treatment of psychotics. The original Freudian basis of the transference phenomenon, namely, that a positive transference was ultimately sexual in origin, is not accepted. The writer believes (following Horney) that the patient-physician attachment is not one merely of repetition of past feelings or experiences, but one that comes about through establishing a human relationship. In the reconstruction, with the analyst, of the atmosphere which obtained in childhood, the patient discovers that part of himself which was originally repressed. Herein lies the curative process.

Eissler (1943) discusses the limitations of psychotherapy in schizophrenia and focusses attention upon the prerequisites of such therapy in the psychiatrist himself. The therapist must accept the patient's delusion and the role assigned to him by the patient, and enter actively into the patient's imaginative production, like an actor on the stage. The entire gamut of emotions, from hatred to love, should be at the psychiatrist's disposal and should be applied in accordance with the patient's needs. Difficulties arise from the conscious and unconscious attitude of the psychiatrist and the patient's interpretation of the psychiatrist's awareness of his needs as insincerity. The need for an active co-operation between the patient's and the psychiatrist's unconscious, according to Eissler, makes the therapy of schizophrenics a matter of chance. The schizophrenic senses the degree to which his world is accepted and feels hurt and repelled when he is loved because he is sick or unhappy or when his language is spoken in order to help him. This limitation of contact is, for Eissler, an unsolved problem. He notes that Schwing (1940) considers *love* as the main road of access to the schizophrenic personality; and that Fromm-Reichmann (1939) besides love, believes that *patience* is the prevailing emotion in making contact with the schizophrenic. In using "the entire gamut of emotions" the sophisticated psychiatrist easily loses contact. It is probable that the dilemma would not have arisen had Eissler been able to rely upon intuition—"that psychological function which transmits perceptions in an unconscious way" (Jung, 1933).

Rosen (1946) in treating patients with acute catatonic excitement aided them to establish contact with reality through their relationship with him.

He assumed the identity of the threatening figures and reassured the patient that far from threatening him, they would love and protect him. Contact with the patient was gained through his emotions and through the visual and auditory pathways. Lengthy sessions were necessary if contact was to be maintained and interpretations received. One interview lasted continuously for sixteen hours except for a break of half an hour. In a later contribution (Rosen, 1947) is recorded the successful treatment of thirty-seven schizophrenic patients. The counter-transference, he holds, is like the attitude of the parent to the child, as distinguished from the transference, which is like the attitude of the child to the parent. The therapist, like the good parent, must identify with the unhappy child and be so disturbed by the unhappiness of the child that he himself cannot rest until the child is again at peace. When this relationship is secure any conscious reaction on the part of the therapist will not be misunderstood by the patient. Rosen states that the *sine qua non* for the application of his method is love. Thus Rosen would appear to agree with Schwing and Fromm-Reichmann (see above); and to disagree with Eissler, who considers that the psychiatrist should, on occasions, employ hatred and other emotions as well as love. Federn (1947), believes "that the relieving agency in Rosen's direct psychoanalysis lies in the positive transference and the participation of the psychiatrist in the psychotic reality of the patient. Rosen, in speaking of his work in a lecture given in London in 1949, and not yet published, made it clear that he was far from being dogmatic about the curative factors in his work. He agreed that the transference was central in every successful treatment and that it involved an active (and reciprocal) emotional situation.

Rubé (1948) emphasizes the importance of psychological factors in the genesis of schizophrenia; and the preponderant part played by psychotherapy at critical periods in treatment by insulin shock and other methods. Many psychiatrists, we read, become almost panic-stricken at the idea of using psychotherapy in schizophrenia. Psychotherapy is here used in a wide sense—as a conscious and deliberate effort, by doctors and nurses, to adapt themselves to the needs of the patient. Technical efficiency is not enough: it must be supplemented by "moral fitness." When nurses are not carefully selected results are inferior. It was observed that no schizophrenic ever seemed to dream during normal sleep, but dreams appeared during convalescence and often referred to those concerned with the conduct of the illness.

Whitehorn (1948) indicates the complexities involved in the attempt to study psychotherapy scientifically. The student can learn little of the actuality of psychotherapy from the ward round or lecture, and the literature is often marred by the emotional reaction of psychotherapists; while those trained in one or other of the "schools" are apt to develop a doctrinaire bias. This colours their formulations, which may be presented as demonstrations of psychogenic aetiology. Whitehorn points out that no treatment can succeed without appreciation of the patient as a person, of the patient-doctor relationship and of "good timing" in the strategy of therapy.

Bierer and Ström-Olsen (1948) conducted experiments in the mechanical recording of diagnostic and therapeutic interviews. The purpose was to

improve teaching and research methods in psychotherapy. An inhibited patient asked to be left alone when the record was replayed, and thereupon produced a mass of aggressive material. So the procedure was of value in therapy and had the advantage of saving treatment hours. Further, the psychiatrist on hearing the record could criticize his technique. A medical audience was favourably impressed by the possibilities of this experiment.

Menninger (1944), aware of the role of nurses in treatment, arranged a series of lectures for them covering aetiology, management and treatment—particularly persuasion and suggestion. The co-operation of nurses (especially when psychiatrists were few) saved the time of the doctor and also provided useful information.

Using questionnaires and interviews Kahn, Redlich and Keller (1945) attempted to evaluate the attitude of medical students towards psychiatry and psychiatric teaching. In consequences, teaching methods were improved. Many students after attending a course of lectures believed they could carry out the treatment of uncomplicated disabilities. One, less optimistic, said "he could start (psychotherapy) but not finish it." Not all psychiatrists are so clear sighted.

II.

Marion Richardson (1948), by her enthusiasm for the production of imaginative art, has opened a new field of treatment in mental illness. Her emphasis was on the value of the child's own inner vision. She never imposed the adult sophisticated view on the child, but elicited from him what he himself saw. Many teachers imbued with her ideas are now working in mental hospitals and co-operating in the treatment given by the medical staff. The patients are guided to express themselves vigorously in purely aesthetic terms. However much of symptomatology the doctor may elicit from the drawings and paintings, the pleasure and happiness generated in patients by the mere act of applying colour to paper, and thus realizing their inner visions, is very great. The release afforded by the actual painting is so marked that patients should be encouraged to pursue this activity when they cease to be patients and return to their usual work. Imaginative art affords an understanding of immaterial needs. It is much more than a technical aid to the elucidation of symptoms.

Dax (1948) believes that the art sessions held at Netherne Hospital made a large contribution to the good results of treatment. Painting is prescribed as a form of treatment because of its value in giving emotional release. It is also of assistance in psychotherapy as a means of elucidating symptoms and thus shortening treatment. This writer adds, as though it were of secondary significance, that sometimes emotional release may be gained by the drawings alone. Yet this is probably far and away the most important part of the art therapy. He states that the patient's pictures are surrendered to the doctor, as they are necessary for treatment purposes—presumably of other patients. This is open to question. The patient has put much into his work; it has a value for him and should be retained by him.

Adrian Hill (1945), whose work at Midhurst Sanatorium is so well known, has much to say on art therapy which is applicable to all patients. The

benefit of such creative diversion in preventing unhappiness and in combating what is described as "the neurosis of the sufferer," provided a significant instrument in the treatment of disease.

Petrie (1946) invites collaboration between the artist and those dealing with the sick. She is probably right in her contention that psychiatrists are not acquainted with the art of "normal" persons and consequently are apt to read too much into the drawings and paintings of their patients, and so miss the aesthetic and creative qualities which have curative power.

Dunnett (1948) noted that the teaching of art in an evacuation school for boys—some of whom were "mentally deranged" and maladjusted—increased a growth of feeling, a sense of freedom and self-respect. The boys lived through their peculiar experiences by expressing them spontaneously in pictures and found release from disturbing thoughts. The therapeutic value of this work was clearly observed in improved behaviour.

Churchill (1948) found in painting "an alternative outlook" providing "new mental food and exercise." "I know of nothing which, without exhausting the body, more entirely absorbs the mind. Whatever the worries of the hour or the threats of the future, once the picture has begun to flow along, there is no room for them on the mental screen. They pass out into the shadow and darkness. All one's mental light, such as it is, becomes concentrated on the task."

III.

Moriarty and Weil (1943) combined E.C.T. and psychotherapy. Others had done so earlier, but had applied E.C.T. grudgingly to the neuroses and for the most part to patients with stubborn and chronic conditions. Paradoxically, when shock therapy had been employed, the importance of psychotherapy had receded. This was a bad blunder. Without psychotherapy the improvement gained by E.C.T. was soon lost. The total effect of combined E.C.T. and psychotherapy is considered to be greater than the sum of its component parts. Kalinowsky and Hoch (1946) consider that the proper place for E.C.T. in the psychoneuroses has not yet been established; and that, with the exception of psychoneurotic depressions, E.C.T. as a treatment for neurotics is, on the whole, disappointing.

Sargant and Slater (1948) believe that psychotherapy should precede, accompany and terminate physical therapy, not only in psychiatric but in all medical and surgical disorders. Psychological and somatic methods should be complementary. The somatic approach, in their opinion, is only capable of improving the instrument that is in our hands, and psychotherapy should have something to say on the aim towards which it is directed.

Milligan (1946) using E.C.T. in the treatment of the psychoneuroses, found its greatest value with two groups of patients: those with long-standing and those with recently acquired symptoms who had not responded to psychotherapy. The former derived most benefit. The intensive method—up to four convulsions daily—was frequently used. Confusion, amnesia and complete disorientation followed. As the patient emerged from the confusional state, simple psychotherapy in the form of explanation and reassurance was given.

Fordham (1946) contrasts the effects of analysis and E.C.T. in treatment. The methods worked in opposite directions. E.C.T. produced an adaptation based on an infantile mechanism and prevented the development of the individuation process upon which the success of the analysis depended. While the convulsions produced temporary improvement in social adaptation they worked against a cure, if by cure is meant becoming whole or individuated.

Sands (1944) advocates the combination of modified insulin treatment with psychological methods. In conditions of morbid anxiety and of hysteria a 60 per cent. recovery rate is reported. Obsessional conditions were resistive to the treatment.

Horsley (1943) introduced the term *Narcoanalysis* for a new technique in short-cut psychotherapy. As long ago as 1931 he experimented with various basal narcotics and sought to combine biochemical and psychodynamic concepts. The author has had a wide experience with narcoanalysis in hospital and out-patient clinics and devotes a chapter to the place of narcoanalysis in psychotherapy.

Grinker and Spiegel (1945) recount their therapeutic experiences with combat soldiers overseas and returnees suffering from war neuroses. The two groups are intimately linked. Psychotherapy with the combat soldier resolved itself into an attempt to force the ego to exert pressure on the welling-up anxiety, which was thereby held in check. This led to cumulative strain upon the ego of the individual kept in a situation which automatically stimulated more anxiety. Consequently, neuroses became overt only after the return home. The reason lay, not in the external stresses of combat, but in the military necessity of bolstering the ego's defences against anxiety rather than enabling the ego to control and bear anxiety. Psychotherapy amongst returned soldiers should be directed towards the latter aim, particularly towards the release of unconscious tensions concerned with anxiety. For quick results the authors employed narcosynthesis (sodium pentothal) with about half the patients.

Grinker (1946) compares excessive sedation to the mechanical restraint of the past. Sedatives are often prescribed to keep patients quiet and so relieve the physician from the responsibility of coping with complaints he is incapable of understanding or treating. Sedatives should be given only to further the influence of dynamic psychotherapy and never to hide the symptoms from the doctor and his patient. Indications for using the barbiturates and other preparations are given.

Rosenberger and Moore (1946) reported the treatment of hysterical deafness by pentothal and suggestion. Intensive therapeutic efforts were continued for days or weeks after narcosynthesis. The results were spectacular: there was no evidence of regression in any patient after a month in hospital.

Plaut (1948) registers a plea against any treatment that fails to allow the patient to develop through his illness. He writes of those suffering from endogenous and reactive depression—if they can, indeed, be differentiated. It is fallacious to treat the one with E.C.T. and the other by psychotherapy. Treatment rests on philosophical considerations and not on aetiological classification.

Rickman (1948) maintains that the use of sedatives, shock therapy, surgical

interference or certification in the treatment of hospital in-patients is not incompatible with psychoanalytical principles provided that every event is referred back to the transference situation.

IV.

Barrie Murray (1949) has produced a concise monograph upon the physical expression of emotion. About 60 per cent. of illness seen in a medical out-patients' clinic is entirely or predominantly psychiatric in nature. By adopting a detailed procedure of history-taking and clinical examination, many unsuspected abnormal physical conditions—important to the patient and therefore to the doctor—have been discovered. The main emphasis is on "effort syndrome," which acquires a wider connotation than is customary. The essentials of hysteria are all present in effort syndrome and in other psychosomatic manifestations. The ever-present fear situation receives the suggested idea which may arise from a previous physical illness of the patient's or of some member of his family.

While the treatment should be psychotherapy, prophylactic treatment is important, and details of this are given.

Scott (1948), discussing the problem of ego structure, advanced the structural concept of a "body scheme" to describe the conscious and unconscious integration which exists before the split into external world, body and psyche occurs. In individual analyses the illusions of the previously rigid boundaries between mind, body and external world are replaced by more useful ways of living. He believes that this concept may be of value in linking psychoanalytic theory to developments in neurology, psychiatry, psychology and related sciences.

West (1946) gives case-histories depicting the characteristic features of ulcerative colitis. The treatment was a combination of psychotherapy and physical remedies. A method of approach to the psychogenic features in physical illness is described. An early diagnosis, followed by psychotherapy, may well avoid a dangerous organic malady. The reports show to what an extent the bodily machinery is at the mercy of ideas; and the high degree of reversibility which exists in psychosomatic illness when psychotherapy is used in time.

Sperling (1946) provides a psychoanalytical study of ulcerative colitis based on the case-histories of children. The literature of psychoanalysis contains few papers on this topic, although the psychogenic features of this malady have frequently been noted. Early frustration was experienced in consequence of ambivalence in the mother. Her unconscious destructive impulses towards the child were rationalized by the opinion that the child would do better away from home. The children reacted with hostile attachment and intense need to retain the position of the baby. Psychoanalysis of the child presents difficulties. The mother, therefore, should have treatment—or even better, the prospective mother.

Groen (1947) paid special attention to the character structure of patients with ulcerative colitis and particularly to the emotional conflicts that preceded the outbreak of the disease. The conflict was specific—an acute loss of love

with humiliation. Psychotherapy was in two parts: an emotional catharsis followed by encouragement. This superficial treatment was remarkably successful. Psychosomatic medicine provides an explanation of the cause and a method for the treatment of this serious disability.

Lorand (1943) contributed a detailed survey of the treatment by psychoanalysis of a girl with anorexia nervosa. Success in treatment lay in working through the early attachment to the mother. The analysis differed from the so-called classical treatment. These patients are unwanted children and cannot form an attachment without arousing the dread that—as in infancy—it may collapse. The transference relationship is, therefore, unusually difficult.

Nicholson (1946), in a study of 93 obese patients, demonstrated emotional problems in all of them. Superficial psychotherapy, without dieting or medication, produced a higher percentage of successful results than other methods studied. These results, it is held, establish the fact that emotional tension and psychoneurosis will, in certain people, produce obesity.

Richardson (1946) also found that obesity may often be regarded as the physical expression of a neurosis; and that the reason for the accumulation of fat and for the difficulty in getting rid of it, can usually be described in psychological terms. Fat is used by many women as a barrier against men and marriage, and so attempts at reduction of weight encounter psychological resistance. Psychotherapy is advised. It must be highly individualized and much depends upon the doctor-patient relationship.

Drefus (1948) found that many obese female patients had experienced severe emotional trauma during the German occupation in France. Psychological treatment with a controlled diet and diuresis relieved the condition.

Weiss (1942) points out that the heart has been the traditional seat of the emotions, that no other organ is used so frequently in a symbolic way to refer to love and hate, and that the majority of patients with "heart" symptoms have healthy hearts but unhealthy emotions. When there is no organic disease the illness should be diagnosed and treated as an anxiety neurosis with cardiac manifestations. A knowledge of psychopathology is essential and in particular a familiarity with the manner in which emotion is expressed when the demands of life are "taken to heart." Professor Weiss makes valuable comments on the differential diagnosis of cardiac disorders.

Jacobson (1946) recounts the treatment by psychoanalysis of a patient who remained sterile despite exhaustive treatment by endocrine and other preparations. The clinicians regarded further treatment of the infertility as unpromising. After eight months of analysis the patient became pregnant and later gave birth to a child. The possibility that the cure was due to a coincidental spontaneous recovery is considered, but rejected.

Malleson (1942) contributes a paper on the management and psychogenesis of vaginismus. The essence of the treatment is explanation and persuasion. Many patients with vaginismus have been "conditioned" to expect pain in the pelvic region by the use of the enema, the suppository or the old-fashioned soapstick. Soap in the rectum (as in the eye) is painful. The rectal, vaginal and urethral orifices develop from the original cloaca and possess the same innervation, and in young children the sensations arising in these organs are

largely undifferentiated. The child who has dreaded the introduction of an object into the rectum would respond with shrinking to the actuality of coitus. The treatment is brief—one interview is often sufficient. Smail (1943) recognizes a distinct group of patients with vaginismus and dyspareunia, and advises psychological treatment.

Loewenstein (1947), while aware of the value of psychotherapy in psychogenic impotence, had the all-too-familiar experience of seeing patients who were resistant to the most thorough psychological treatment. In consequence he has introduced an ancillary method of treatment, namely, mechanotherapy, in the form of a coitus-training apparatus. The appliance supports the flaccid penis and coitus is made possible. Patients report that soon they cease to notice the apparatus, which is not inconvenient to the partner. Normal erection is often quickly re-established and the extraneous aid is then abandoned. This method will appeal to many as an alternative to artificial insemination.

Hoskins (1944) holds that the essential psychosomatic nature of clinical endocrinology is evident in the climacteric disorders. The psychological and the organic make-up of each patient must be studied simultaneously. Anxiety is prominent and so is the over-stimulation of the sympathetic nervous system—caused by anxiety. The therapeutic problem is to alleviate the anxiety. The menopause pronounces a verdict of senescence—a threat to the ego—and the waning capacity affects “the self-regarding instinct.” Some require prolonged analysis, but with the well-integrated simpler measures suffice.

Backus and Mansell (1944) found explanation, education and suggestion effective in treating soldiers with nocturnal enuresis. Exercises in sphincter control in the daytime were linked with nocturnal control which was fortified by suggestion. Hypnosis was tried but abandoned.

Wolff (1948), in a study of the migraine syndrome, gives prominence to therapeutic management. While the bodily features of the complaint play a secondary role, they are not neglected. The clinical problem centres around the prevention of pernicious moods, tension, dissatisfaction, feelings of frustration, and obsessive preoccupation with work or responsibilities. Therapy includes reassurance, catharsis and especially re-education. A personality study facilitates a correlation between morbid traits and the migraine.

Wolff also gives advice on the management of those with chronic post-traumatic headache. Of great importance is the total reaction of the patient to head injury. An anxious physician is a menace to these patients. He creates an atmosphere of impending catastrophe which the patient adopts as his own.

Hilgard and Szurek (1943) give a careful history of the successful treatment by psychotherapy of a choreic syndrome classified as Sydenham's chorea. This is of interest as there have been few published records of psychotherapy in chorea, although the psychological features in the condition have often been emphasized.

In the previous decade Hochheimer (1936), in a survey of the literature dealing with the psychology of the choreic patient, believes that the boundaries of clinical psychology will be finally determined by defining the brain-mind

relationship. The psychological and physical elements of disease will then be combined in one picture.

Ascher (1948) describes the treatment of Gilles de la Tourette's disease (widely spread spasm, explosive utterances) based on a study of five patients. Psychotherapy was the only form of treatment. Organic involvement of the C.N.S. was excluded. One patient recovered and in two there was no improvement. The treatment of the others was terminated prematurely, but showed some improvement in one and "increased comfort" (without symptomatic change) in the other.

Roth (1946) gives a case report of a patient with narcolepsy and cataplexy to illustrate two disputed points—the relationship of narcolepsy to the convulsive disorders and the importance of emotional factors in its pathogenesis. He argues that the psychological processes have neurophysiological counterparts, as detected in the EEG record and in the clinical symptoms, and that in some narcoleptics there are neurophysiological similarities to the convulsive disorders. This is claimed to be the only reported example of narcolepsy in which a *petit mal* pattern appeared in the cortical cerebral discharges.

Auerbach and Gliebe (1942) consider spasmodic torticollis to be a psychogenic disorder. Five case reports are given. With one exception all recovered with psychotherapy. Special attention was given to the emotional atmosphere when the symptom first appeared. The symbolic meaning of torticollis, as turning away from a problem, was apparent. The authors refer to the article by Halliday (1937), who showed that feelings are constantly expressed by positions of the head and neck.

Pai (1947) considers that every person with "writer's cramp" for which there is no organic cause should be treated as a psychiatric patient. "Writer's cramp" is included amongst the Dangerous Trades for the purpose of the Workmen's Compensation Act. Pai (with many others) regards it as a symptom of neurosis, and he employs hypnotic suggestion.

V.

Bion and Rickman (1943) used the term "group therapy" to describe the planned endeavour to develop in a group the forces that lead to smoothly-running co-operative activity. This is in contrast to the commoner conception of group therapy as a therapeutic session employing explanation with reassurance and giving an opportunity for the cathartic effect of public confession. The structure of groups and the interplay of forces within the groups are considered to be subjects worthy of special investigation. A different aim is that of Gibbs (1945), who saw in group play therapy a technique for treating the nervous disorders of children. The co-operation of parents was an important element. The group was small—three or four children. The aim was not "socializing" play, but treatment for individual disabilities in a group situation.

Blair (1943), working under the pressure of war conditions, devised a speedy and effective method of group therapy. Each patient on arrival in hospital was given a type-written sheet of "exhortations" conveying reassurance and encouragement, and on the next day this was discussed in a personal interview.

Most patients were thought suitable for the group therapy, which took the form of lectures on elementary psychology, anatomy, sexual problems, fear and self-treatment.

Skottowe (1944) worked on similar lines, but chose groups of patients with like complaints, such as anxiety with effort syndrome. A series of explanatory lectures and seminars comprised the treatment.

Maxwell Jones (1948) considers that group methods of treatment are still too undeveloped to have evolved any specific treatment techniques. He describes a form of group therapy in which acting was used to promote re-education and catharsis. Social situations which have created emotional difficulties for the patients were re-created and acted. The subjective and objective reactions were then discussed in order to evoke a more desirable pattern of behaviour when the patient again faces this social situation. The catharsis is achieved by placing the patient in a situation resembling the original experience and asking him to re-live it.

Mitchell and Zanker (1948) employed music as a medium of group therapy—much as painting and psychodrama have been used. The purpose was the improvement of interpersonal relationships. Weekly sessions were held and gramophone music, supplemented by active participation in a percussion band or singing, was followed by group discussion. This was not limited to musical topics—any problem could be raised. A specific response to different musical styles was noted. This was thought to have a bearing upon group cohesion and relationships. Altshuler (1944) considers music of special value in dispelling the phantasies and hallucinations of psychotic patients.

Harwood (1946) found that 26 per cent. of a group of patients in hospital with war neuroses could be returned fit for military duty by employing only occupational (convalescent) therapy.

Scheidlinger (1948) places the re-creation of a family setting as the primary dynamic element in group psychotherapy. The therapist assumes the role of a parent figure and the other members represent the patients' siblings. The competition of the siblings for parental love is resolved through the process of identification and the group then evolves mutual love and protection.

Taylor (1949) in an account of a visit to the Danish Psychopathic Prison at Herstedvester, describes the work there as the first successful attempt at the scientific treatment of human wickedness. Sentences are indeterminate, but a 50 per cent. cure-rate is achieved. The patient is led to see that he is responsible for his own future. Psychotherapy is brief and carefully timed. The offender is shown why he is feeling and behaving as he does. Many come to accept the possibility of a non-egocentric universe. The experiment is a combination of group therapy and individual treatment.

Bromberg (1948) advocates *attitude therapy* in dealing with individual offenders. It is aimed particularly at the unreasonable antagonism exemplified in the antisocial motives which impel the offender. The stabilizing influence of the doctor helps to replace early emotional deprivation from which the immature psychopathic characters derive their rebelliousness. The difficulty, however, lies in translating theory into practice. The status of psychotherapy in criminology—at any rate in America—only allows detailed individual treatment as

an exceptional measure. But psychotherapeutic principles may be of value in the management of prison life, especially in dealing with disciplinary matters, where antagonisms may so easily be fostered by hasty action. Bromberg believes that the use of psychotherapy with criminals finds its main justification as an instrument of research into psychological mechanisms in criminals.

The psychotherapeutic treatment of persons convicted of sexual and unnatural offences was reported upon by a Standing Advisory Council appointed under the Scottish Home Department (1948). Amongst the recommendations made was the formation, under special conditions, of a special psychotherapeutic centre within the prison system. In this proposal they were guided by the experience of similar work in Wormwood Scrubs prison, described by East and Hubert (1939).

The Commissioners of Prisons and Directors of Convict Prisons (1947) refer to the treatment of prisoners in Wormwood Scrubs prison by individual psychotherapy and group therapy. The latter method had the effect of shortening treatment, but was not used to replace individual analysis.

Kowert (1948) described the treatment of a group of patients before a medical audience of fifty doctors, medical students, psychologists and social workers. The old-fashioned notion of secrecy and confidential interviews has become unnecessary, we are told, because the social resistance to psychotherapy is less than it was in the days when Freud began his work. If group therapy is possible then why not group therapy as a demonstration in teaching group therapy?

The patient sat in the first row of the amphitheatre facing the doctor, with the audience at one side. It is claimed that this demonstration—an interlude in group therapy conducted elsewhere—was not “psychonoxious,” but valuable to the patient, and that group psychotherapy demonstrations permit the confirmation, by observation, of therapeutic claims.

It will be evident from these few references that there is little or no uniformity in the theory and practice of group therapy. Research into group dynamics, teaching, therapy, the shortening of therapy, and social adaptation have all been objectives. A multiplicity of procedures and hypotheses have been advocated. All have their protagonists and their critics. A summary of the more important observations is to be found in the papers on group therapy published in the *Proceedings of the International Conference on Medical Psychotherapy* (1949). No doubt a degree of unification in method will be reached in the fullness of time and this (let us hope) will rest upon established principles in psychopathology. But so long as human beings differ typologically there will be divergence in the theory and in the practice of group therapy—and individual therapy.

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INSULIN THERAPY.

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INSULIN therapy, introduced by Sakel (1935) spread to all parts of the world during the decade following its introduction and the beginning of the period under review. It has continued to be a potent stimulus to research, and investigations have proceeded on the assessment of its therapeutic value, prognostic factors, and on biochemical, physiological, psychological and pathological changes accompanying or following hypoglycaemia.

The early hope that such studies would reveal the nature of the fundamental disorder in schizophrenia and enable a specific therapy to be evolved has not yet materialized, but continuing researches are significantly advancing our knowledge in this important field.

It will be convenient to consider publications relating to insulin therapy under the following headings :

1. Technique and management.
2. Complications.
3. Physiological, biochemical and psychological aspects.
4. Therapeutic results.
5. Prognosis.

TECHNIQUE AND MANAGEMENT.

Variations in technique and management have been described, but no major advances can be reported. The publications relate to method of insulin administration, termination of coma, the number and depth of comas necessary, subcoma insulin therapy, and the combination of insulin coma treatment with various other therapeutic techniques.

Intravenous Administration of Insulin.

Spencer (1947) reviews the literature on the subject, and describes his investigations on the effects of intravenous injection of insulin. He finds that intravenous insulin saves time in treatment amounting to about 30 minutes each day, and that a milder hypoglycaemia state can be induced with less insulin with a greater possibility of spontaneous awakening by the patient. It has disadvantages, however, in that there is a greater incidence of spontaneous major epileptiform convulsions ; that anaphylactoid shock may occur in patients sensitive to insulin, and that more insulin is required to produce the deepest hypoglycaemic states. He concludes that the advantages of intravenous insulin in Sakel's treatment are not sufficient to justify its use.

Number, Depth and Duration of Comas.

There is considerable variation in the duration of treatment and the number and even the depth and duration of comas by different physicians employing insulin coma therapy for schizophrenia.

Freudenberg (1947), surveying 10 years' experience with insulin therapy, concludes that the production of comas is essential. The comas must be of sufficient depth, must be clearly defined, and a certain minimum number administered to achieve therapeutic success. He considered that 50 comas should be aimed at even if the patients remit early in treatment. Freudenberg's results show that the number of patients with total and social recovery is definitely higher when 30 comas and over are given, compared with those given less than 30 comas.

Levy and Perry (1947) keep the patient in coma for one hour, whereas with Horwitz and Kalinowsky (1948) the duration of maintained coma is four hours.

In order to produce deeper and longer comas Bond and Shurley (1946) rapidly increased the dosage of insulin, starting with 50 units on the first day, and on successive days 100 units, 200 units, 400 units, 600 units and 1,600 units. When stupor occurs within $3\frac{1}{2}$ hours after injection the dosage is levelled off, and when deep comas are obtained the dosage is reduced equally rapidly in order to determine the minimum dosage needed to produce deep stupor. The patient is maintained in deep coma two hours daily. There were four deaths in 400 patients, and none in the year prior to publication. Death in two patients was due to irreversible coma. Termination was always carried out by intravenous administration of glucose. Clearly this method should only be tried by those with considerable experience in insulin therapy.

The coma dose of insulin must be determined for each individual by graduated increases. The amount of insulin needed varies with the depth of hypoglycaemia desired and the resistance of the patient to the hypoglycaemic effects of insulin. Insulin resistance was studied by Freeman (1946) in groups of normal and psychotic soldiers. He gave insulin amounting to 0.1 unit per kilogram body-weight. It was found that insulin resistance measured by the degree of hypoglycaemia was a feature of many types of psychiatric disorder. An interesting finding was that insulin resistance was as great in early as in chronic schizophrenics. Somogyi (1948) found that periods of hypoglycaemia tend to be followed by a period of insulin resistance, and considers that this might be due to stimulation of pituitary and hypothalamus by hypoglycaemia.

According to Stell (1945), insulin resistance can sometimes be overcome by a small number of metrazol convulsions.

Goldberg and Jefferies (1946) suggest that nicotinyl taurine may provide a relatively non-toxic synergist to reinforce the insulin effect in insulin-resistant cases.

Sometimes when intravenous administration of glucose is indicated, conditions may make injection into veins very difficult. Such a difficulty may be overcome by a new technique of terminating hypoglycaemia by sternal puncture, described by Dalgaard (1947). The method consists of inserting a trocar and cannula in the marrow of the corpus sterni at the level of an intercostal space. The trocar is removed and aspiration made by means of a syringe partly filled

with glucose saline. The withdrawal of blood mixed with marrow attests correct placement. Dalgaard recommends that the chest be X-rayed before starting treatment to rule out such conditions as aneurysm.

MODIFICATIONS OF INSULIN THERAPY.

Subshock Insulin Therapy.

Insulin in small doses had been used in psychiatry before the introduction of insulin shock therapy, chiefly to increase weight in undernourished patients. This method was overshadowed by insulin shock therapy until its revival and elaboration during World War II as the modified or subshock insulin treatment of war neuroses. Subshock insulin therapy has been used in the treatment of neuroses, psychoses and acute alcoholic intoxication.

Neuroses.

Sargant and Craske (1941) described their technique of giving insulin in gradually increasing doses short of producing coma in neurotic soldiers, and subsequently the method became widely used in the treatment of psychiatric patients during World War II.

Sargant (1949) reviewed his experience in the use of the treatment in 1,000 cases, and stresses that the method has real limitations. He regards the tendency to employ modified insulin as a complete treatment of the neuroses as unfortunate, since psychotherapy is the critical factor. Sargant considers that patients with a severe loss of weight and a persisting tension may respond more quickly when modified insulin treatment is combined with psychotherapy.

Fox (1945) found subcoma insulin treatment of value in promoting the rapid rehabilitation of soldiers with symptoms of acute panic or protracted states of anxiety. He found that retention of consciousness was helpful in rehabilitation, that patients were able to speak more freely of experiences not previously disclosed, and the recall was less disturbing than with amytal or pentothal narcosis.

Kelley and Thompson (1947) described their impressions and conclusions drawn from the results obtained with subshock insulin therapy in 5,000 patients seen during World War II. They conclude that the method is of value in acute reactive disorders of sudden onset with psychosomatic symptoms, especially loss of weight. Chronic neurotics do less well. The authors conclude that the mode of action is not known, but that gain in weight and the general regime of treatment may have potent suggestive value.

Sullivan (1948) finds that neuroses of severe anxiety tension type respond well to subshock insulin therapy. Such symptoms as hyperidrosis, neurodermatitis, emotional instability, depression, acute panic, tremulousness, startle reactions and battle dreams begin to disappear in the fifth or sixth day of treatment, and patients gain weight and become more cheerful, relaxed and co-operative.

Hohman and Kline (1946) found the method useful in the treatment of a group of 37 naval personnel suffering from anxiety states with depression and hypochondriacal features. They found that anxiety and depression usually

begin to subside by the fourth day, and psychosomatic symptoms as a rule were the last to show improvement. The authors believe that the production of hypoglycaemia by subshock doses of insulin stimulates the sympathetico-adrenal mechanism at the hypothalamic level, thus restoring autonomic balance, re-establishing homeostasis, and probably influencing the cortex *via* the hypothalamus.

Teitelbaum *et al.* (1946) attempted to evaluate the therapeutic value of modified insulin by comparison with other methods of treatment. A group of 201 men were divided into four groups. One group on a general ward received group therapy only, the second received subshock insulin in addition to group therapy, the third received sodium amytal sufficient to produce drowsiness comparable to that produced by subshock insulin, and the fourth group received a placebo. In all groups weight loss was a marked feature, and only the insulin groups showed a tendency to cause weight gain.

Improvement as measured by a percentage diminution in the number and severity of symptoms was, in insulin treated group, 60 per cent.; in group given placebo, 54 per cent.; general ward given group therapy, 51 per cent.; and sodium amytal group, 50 per cent. The authors concluded that since the differences do not exceed three times the standard error, insulin had no specific effect in producing symptomatic relief. They stated that no correlation existed between weight loss before treatment or weight gain during treatment and degree of improvement.

Sargant and Slater (1947) questioned some of these findings. They point out that Teitelbaum and co-workers demand a very high standard of significance before accepting the materially greater improvement under insulin than under other treatments as proof of its efficacy. By means of analysis of variance, Sargant and Slater arrive at the conclusion that there are more than 19 chances to one that the greater improvement in insulin is not due to chance.

Further statistical analysis, using Teitelbaum's data, showed that (1) severity of symptoms was almost certainly related to the amount of weight lost; (2) degree of improvement was probably related to weight gain; (3) it is probable that insulin is a better method than the other three.

Martin (1949) compared the results obtained by treating a group of 210 cases of anxiety neurosis with subcoma insulin with a group of 170 similar patients. Both groups participated in a general psychotherapeutic regime. The insulin group showed a greater degree of improvement. The best results were obtained with the less predisposed patients with an illness less than 10 months' duration, and with battle stress as a precipitating factor.

Gayle and Neale (1949) similarly found that subcoma insulin therapy used in 136 patients at the neuropsychiatric department of a general hospital was found to be valuable in relieving tension symptoms, shortening the period of hospitalization, and rendering the patient more susceptible to psychotherapy.

We may conclude that there is evidence that modified insulin therapy can be valuable in the treatment of neuroses, particularly by its sedative action in relieving anxiety, tension, depression and psychosomatic symptoms. It is generally agreed that modified insulin therapy is best used as a part of a general psychotherapeutic regime.

Psychoses.

Polatin and Spotnitz (1946) used subcoma insulin therapy in combination with electroshock in the treatment of schizophrenics to see if the apparent rapid clinical improvement with electroshock could be maintained. Insulin was started after the sixth electroshock and given concurrently. Usually the treatment comprised 20 electroshock sessions and 11 weeks of subshock insulin treatment. In a group of 30, 60 per cent. were described as much improved, 17 per cent. improved and 23 per cent. not improved. It was noted that poor results occurred in patients who showed belligerent reactions during hypoglycaemia.

Sullivan (1948) used subcoma insulin treatment twice a day seven days a week for 3 weeks in the treatment of schizophrenics, and advocates that the method be used in all psychoses with schizophrenic or depressive symptoms, and states that electroshock given three times a week for four weeks will increase the overall rate of improvement. These findings cannot be regarded as conclusive proof of the value of the treatment, as the results are not fully controlled.

Beaudoin, Joyeux and Quercy (1948) used the method of combined subcoma insulin treatment and electroshock therapy described by Polatin and Spotnitz (1946) for the treatment of schizophrenia. In a series of 18 patients, only two recovered, and one of them relapsed shortly afterwards; four patients relapsed after transient improvement, and in nine patients there was aggravation of symptoms. They conclude that the method is not as satisfactory as claimed by its originators.

Sargent (1949) considers that the substitution of modified insulin treatment for a full insulin coma regime in early schizophrenics may be doing a grave wrong to many patients. It was, in fact, found that modified insulin therapy in early schizophrenics may prolong treatment and suffering and a degree of deterioration may supervene.

It may be concluded that subcoma insulin therapy, even in combination with electroshock, is of very doubtful value in the treatment of schizophrenia.

Acute Alcoholism.

Vassaf and Hall (1946) found insulin, given in doses of 10 units two or three times daily during the gradual withdrawal of alcohol, a valuable therapeutic adjunct in the treatment of alcoholism.

Thimann and Peltason (1947) also found insulin in subshock doses valuable in treating acute alcoholic intoxication. Insulin was found to have a sedative and sobering effect. The dosage varied from 10 to 80 units (average 60 units). The time lapsing between insulin and dextrose administration varied from $\frac{3}{4}$ to 4 hours.

Insulin Coma and Convulsive Therapy.

It was a natural development for convulsive therapy to be used with insulin therapy in the hope of improving the efficacy of the latter.

Freudenberg (1947) used electroconvulsive or cardiazol convulsive therapy in combination with insulin coma treatment when manic-depressive features, marked excitement, restlessness or stupor were present. Also if there was no

improvement with insulin coma therapy alone after 20 comas, convulsive therapy was added.

Smith (1947) finds electro-convulsive therapy useful in conjunction with insulin in the following instances :

1. At the end of insulin treatment when the patient was fearful of facing responsibility, electroconvulsive therapy seemed to produce alertness and greater urge to cope with reality.
2. When no progress was occurring with insulin.
3. Marked resistance to insulin.
4. When patients remained withdrawn and autistic after coming out of insulin coma, electroshock seemed to facilitate better contact with environment.

Horwitz and Kalinowsky (1948) described results of treating a group of 78 schizophrenics with combined insulin coma and electroconvulsive therapy. The electroconvulsion was given 2-4 times weekly, usually at the second half of the insulin coma treatment. They report of the 78 patients that one recovered, 21 were much improved, 28 improved, and 28 not improved.

The patients who responded were those of good prognosis without treatment, and it is difficult to assess the value of the treatment from the data given.

Insulin Therapy and Narcosynthesis.

Levy and Perry (1947) described a method in which sodium amytal gr. $7\frac{1}{2}$ -15 is given intravenously when patient is being brought out of hypoglycaemic coma. The patient is encouraged to talk freely, and the authors consider that inhibitions are removed more effectively than with insulin alone. The treatment is given three times a week, and the information elicited is discussed with the patient the same day. This is a preliminary report on 11 patients, all but one of whom were much improved, at 6 months' follow-up. All were female and mixed in type, but mainly schizophrenics. The group is too small for definite conclusions to be drawn on the precise therapeutic value of the technique.

Stratton, Hobbs and Carscallen (1947) utilized insulin hypoglycaemia and pentothal as aids to psychotherapy. Subshock insulin therapy was given in the morning, and a short therapeutic interview was given to each patient on termination of hypoglycaemia. The afternoons were used for occupational therapy, group activities and psychotherapy. If progress was not satisfactory, pentothal was given in the afternoon following insulin treatment. During pentothal narcosis the patient was taken through his experiences in detail, and was made to reconstruct them when fully conscious.

Insulin Coma and Corpus Luteum Hormone Therapy.

Billig and Bradley (1946) describe a series of patients in whom pre-menstrual exacerbation of psychosis was not relieved, either by insulin or by insulin and E.C.T., but which responded to progesterone administration. The procedure employed was to give 2 mgm. progesterone intramuscularly twice monthly, usually on the 12th and 14th day following the first day of the preceding cycle. Sometimes it was necessary to increase the dose to 5 mgm. each in addition

to a third dosage on the 16th day. The treatment was continued for 12 months. The authors consider that progesterone production might be deficient in cases of pre-menstrual exacerbation of a psychosis, leading to excessive or un-antagonized oestrogenic substances, thus contributing to irregularities of the autonomic system.

Insulin Coma and Psychodrama Therapy.

Insulin therapy is used by Moreno and Schwartz (1948) as a preparation for psychotherapy of psychotic patients. The authors believe that in the first phase of insulin treatment, withdrawal of glucose is a threat to the patient's welfare. The glucose is supplied at the moment of greatest need. The threatening condition appears to be favourable for the expression of spontaneity, and puts them in a favourable state for treatment.

Following the termination of hypoglycaemia, patients were taken to the theatre for a session which lasted from 1½-2 hours, and one or more patients presented a biographical episode or series of episodes which appeared to him and the psychiatrist particularly pertinent. They find that insulin in some patients seems to irritate and so produce a situation unfavourable for psychotherapy. Psychodrama too may be harmful in certain patients.

The authors classify psychotics as :

1. Drama (or act) positive.
2. Drama (or act) negative.

The former respond to action techniques and learn when in action. They reproduce their delusions and hallucinations and externalize them on the stage. The aim of treatment is controlled release of spontaneity.

The latter group are unable to reach action levels by themselves and remain quiet and fixed at a verbal level.

Insulin Combined with Other Therapeutic Techniques.

Various modifications and elaborations of insulin therapy are described by continental authors.

Insulin is given with pyretotherapy by Doussinet *et al.* (1949), who used minute doses of colloidal gold, sulphur or arsenic together with small doses of insulin (40 units on the average) in the fasting patient. The hypoglycaemia often terminates spontaneously, but occasional oral or intravenous glucose is necessary. The authors have used this method in 200 patients suffering from psychiatric disorder.

Bore (1949) combines massive removal of cerebro-spinal fluid, air injection and pyretotherapy with insulin treatment.

It is not as yet possible to assess the value of these elaborations of insulin therapy.

DANGERS AND COMPLICATIONS.

The complications that may occur during deep insulin treatment are varied, but the majority come into the following classes :

1. Neurological.
2. Respiratory.
3. Cardiovascular.

Neurological.

Spencer (1948) in a survey of the literature refers to the following neurological symptoms after termination of the coma:

Slight confusion, persisting after termination of coma, is very common. Stupor may last for periods up to 10 hours; aphasia, dysarthria, echolalia and echopraxia, diplopia, facial paralysis, hemiplegia and epileptiform seizures. These symptoms are transient, usually passing off within $\frac{1}{2}$ to 10 hours.

Post-hypoglycaemic coma (synonyms: prolonged coma, protracted shock, irreversible coma). This is one of the most serious complications of insulin therapy. The term is applied when the patient does not recover consciousness after glucose has been given orally or intravenously in amounts ordinarily sufficient to terminate the coma. The condition is characterized by normal blood sugar or induced hyperglycaemia, changing neurological features, autonomic disturbances and convulsive phenomena (Rivers and Rome, 1944). Hyperthermia, hyperventilation, rigidity and tonic spasms are usually present. The Babinski response may or may not be present, but corneal reflex can usually be elicited (Spencer, 1948). The condition may persist from a few hours to several days, and may result in complete recovery, recovery with varying degrees of cerebral damage, or death.

Spencer (1948) finds that certain factors influence the incidence of post-hypoglycaemic comas. He finds that the majority of comas occur in the first 14 days of treatment, and that the more profound the hypoglycaemia, other things being equal, the greater the possibility of prolonged coma developing. The duration is also important and even comparatively light stages of hypoglycaemia may result in prolonged coma. Post-coma confusion is a warning sign as prolonged coma may develop on the following day, and patients developing such confusion should be given a few days' rest from treatment.

Rivers and Rome (1944) find that age, sex, insulin dosage, depth of preceding coma, were not significantly related to tendency to prolonged coma. The decisive factor they consider is the total reaction of the patient at a given time. They consider that some patients are predisposed to water imbalance, and that these are the ones likely to incur a state of prolonged coma.

Various theories have been propounded to explain the development of post-hypoglycaemic coma.

Rivers and Rome (1944) believe that during deep hypoglycaemia a progressive cellular hydration occurs and consider it to be reversible, depending on certain variables, and accomplished by the restoration of normal dextrose substrate. However, if the point of simple irreversibility is passed, additional agents must be employed to restore the cellular balance, and in cases in which the progressive hydration has been excessive all efforts at restoration of cellular function will fail and death of the cell results.

The authors consider that the marked changes in electrolytes in blood serum accompanying hypoglycaemia and increased cell permeability are probably due to failure of metabolic processes necessary for the maintenance of the dynamic equilibrium of the normal cell brought about by lack of dextrose substrate.

Rivers and Rome (1944) on the basis of their investigations and those of other workers submit the following attractive hypothesis: That in insulin hypoglycaemia with its so-called cellular anoxia, which tends to increase the permeability of the cell membrane and decrease its selectivity, there is an out-pouring of potassium from the cell and a shifting of sodium from the extracellular spaces to the cell, and with this shift of sodium there is an accompanying aliquot of water. If the cellular anoxia continues or increases, there is a progressive loss of potassium and dilution of the cell contents with incoming water to an irreversible point, after which there is complete loss of the functional and frequently the structural integrity of the cell. In such an event the prognosis as well as the clinical picture depends on the number of cells involved and their location. The authors discuss these changes further in relation to the colloid chemistry of the cell, in which gel passes irreversibly to solid phase, explaining the typical pathological picture seen in the brain damage by insulin therapy.

Malamud (1948) describes pathological findings in two cases in which fatal complications occurred during subshock treatment of a schizophrenic and another with delirium tremens. Both cases had typical irreversible reactions. Case 1 had a protracted coma with convulsions and decerebrate rigidity, with an individual dose of 60 units and a cumulative dose of 315 units, and Case 2 had a protracted coma following an individual dose of 50 units. The duration of fatal episode was 60 and 75 hours. These cases stress the contention of Rivers and Rome (1944) that individual factors are important in protracted coma, since neither duration of stupor before administration of sugar nor maximum or cumulative dose of insulin or other measurable factors seem to play a role.

Identical pathological findings were found in both cases. The cerebral cortex and striate body showed a diffuse disintegration of the parenchyma with a pseudolaminar distribution in the cortex, while microglial proliferation and vascular endothelial swelling occurred secondarily. Severe oedema of tissues was noted.

Treatment of Post-hypoglycaemic Coma.

Rivers and Rome (1944) on the basis of the above theory enunciate certain principles of treatment of post-hypoglycaemic coma. Dextrose must be supplied to stop the progressive cellular depletion of sugar. Once the blood sugar has been raised to normal there is no advantage in the continued administration of dextrose. Dehydrating agents should be given in patients who have had a prolonged coma, or in those in whom a prolonged coma is feared. If patient does not respond within 15 minutes of glucose administration he should be given 50-100 c.c. of 50 per cent. sucrose. A beneficial effect is usually found during the next half hour. It was found that the effect of such hypertonic solutions passed off after 3 hours. Therefore sucrose is repeated every 3 hours during the first 24 hours of coma.

Rivers and Rome also give concentrated lyophile serum to reduce cerebro-spinal fluid pressure and to relieve cerebro-cellular oedema. Its effect lasts

about 6–8 hours. Oxygen and CO_2 are given to overcome the alkalosis incident to hyperpnoea.

Stark and Barrera (1949) have had considerable success in terminating comas with potassium. A 10 per cent. solution is given intravenously by means of a 1 c.c. tuberculin syringe with constant auscultation of the heart during administration. The solution is injected slowly at a rate of 0.02 to 0.04 gm. at a given injection. Another injection is not given until normal cardiac rhythm is re-established. Calcium for intravenous injection must be available to counteract side reactions. The authors consider that the fundamental regime for protracted coma should include adequate administration of dextrose intravenously and adequate electrolytes. They consider it advisable to administer potassium prophylactically before insulin treatment, e.g., potassium chloride 2 gm. four times a day during the course of insulin therapy. The authors state that the mechanism for improvement is not known, but the theory of Rivers and Rome described above offers a rationale for the use of potassium.

Respiratory.

Gottesfeld *et al.* (1945) found that pulmonary oedema occurred in 2 patients in a series of 234 cases.

The presence of asthma in one patient and a history of allergy in the other suggested that the allergic factor might be important. The following possible causes for pulmonary oedema in insulin coma were considered: Depletion of glucose in C.N.S. and cerebral anoxia, release of adrenalin with sympathetic stimulation, deprivation of myocardial glucose reserve, progressive tachycardia and elevation of blood pressure and diminished volume output with cardiac dilation.

In both cases there were specific allergic sensitivities prior to the administration of insulin. They consider that allergy may be a factor, although it is difficult to see how this can be claimed on the evidence of two cases, particularly in view of the widespread incidence of allergic reactions in the general population.

Cardiovascular.

Gralnick (1944) found that in insulin coma treatment acute pulmonary oedema with electrocardiographic changes suggestive of coronary occlusion may be precipitated. Its aetiology has been suspected to be a disturbance of the cerebral respiratory centres, local respiratory irritation and failure of the left heart. The pulmonary oedema will often respond quite readily to intravenous injection of hypertonic glucose. Electrocardiographic changes produced during insulin shock treatment may indicate disturbances of the myocardium proper or of the coronary vessels. The presence of mild myocardial disease need not preclude treatment, but should dictate caution.

Weil describes a case which shortly after termination of insulin coma developed acute cardiovascular collapse with cessation of heart action in whom intracardiac injection of epinephrine produced resuscitation of heart beat and recovery. Weil believes that the cardiac changes during hypoglycaemia are due both to the increased return of the blood to the right side

of the heart, and to a central release of parasympathetic activity secondary to cerebral anoxaemia.

Miscellaneous Complications.

Viet (1947) mentions the following as infrequent complications of insulin coma therapy: compression fractures, urticarial reactions, subarachnoid haemorrhage, duodenal ulcer and hepatic dysfunction.

McGrath (1950) described two rare complications of insulin coma therapy which had occurred for the first time in a series of 1,000 cases treated at the Crichton Royal Hospital. The first patient developed attacks of spontaneous hypoglycaemia over a period despite the withholding of insulin. The second patient developed diabetes mellitus within a month of completing a course of insulin coma therapy. It is considered that this patient was genetically pre-disposed to diabetes mellitus.

Gralnick (1946) reports on the effects of shock therapy administered during pregnancy. In one patient insulin coma treatment was given during the second and third months, and the other received both electroshock and insulin during the first five months. Both after a full term of gestation delivered dead babies. He considers death of the foetus to be attributable to the insulin rather than electroshock. The author states that in spite of the risk involved several factors indicated the advisability of shock treatment in these patients. This report indicates the danger to foetus, and the decision whether to apply shock therapy will rest on an assessment of all the factors and risks involved.

Cossa and Lombard (1948) report that poorer results were obtained by insulin therapy in France than before the war, and that excessive purification was responsible for the disappearance of pancreatic principles which might be therapeutically valuable. Porot (1949) finds complications now more frequent and thinks the cause is similar, although this is an impression, and is in no way conclusively demonstrated.

PHYSIOLOGICAL ASPECTS.

Himwich (1944) gives a masterly review of physiological changes accompanying hypoglycaemia. He points out that marked changes occur in the internal milieu during hypoglycaemia, including an increase in cholesterol and serum protein and a decrease in phosphorus, potassium, amino acids, in addition to glucose. He stresses that the brain is the only organ which obtains its energy from carbohydrate alone. During progressive hypoglycaemia, neurological changes occur which follow Hughlings Jackson's theory of the phyletic organization of the central nervous system, according to which the new phyletic and higher anatomical parts of the brain regulate and control the older and lower parts.

During hypoglycaemia after a latent period of some 30 minutes symptoms successively appear which may be described as belonging to five groups:—

1. Cortical phase: The symptoms of this phase include parasympathetic overactivity. Muscles are relaxed, speech is slow, and the execution of voluntary muscular activity becomes more and more

imperfect. There is a gradually developing clouding of consciousness, and orientation becomes impaired.

2. Subcortico-diencephalic phase: During this phase sensations become less discriminated and reflex activity more generalized and less adapted to the specific stimulus. Sympathetic overactivity is marked with dilated pupils, exophthalmos, viscid perspiration and flushed facies. Involuntary grasping and sucking movements occur. Myoclonic twitches may occur, which occasionally pass into clonic movements and a fit. Motor restlessness with aimless activity is a feature of this phase.

3. Mesencephalic phase: In this phase parasympathetic signs reappear, but accompanying muscular spasms there are sympathetic responses such as accelerated heart rate and raised blood pressure. Both tonic and torsion spasms may occur in this phase.

4. Premyencephalic phase: The tonic spasms of the third stage give way to recurrent extensor spasms accompanied by signs of sympathetic overactivity. The reflexes of Magnus and De Kleen may be elicited, and the phase resembles the decerebrate rigidity of Sherrington.

5. Myencephalic phase: This is the most dangerous stage in coma and should not be allowed to continue more than 15 minutes or so, and as soon as recognized glucose should be given. Parasympathetic activity predominates with extreme muscular hypotonia, fall in temperature and absent corneal reflexes.

During recovery the signs and symptoms occur in reverse order, and we again see the phyletic organization of the nervous system in operation.

Considerable research has been carried out on neuro-vegetative and endocrine changes during shock therapy.

Following the work of Hoskins (1946), Hoagland *et al.* (1946), which suggested that schizophrenics were defective in one or more of the numerous physiological and biochemical mechanisms which maintain homeostasis, Parsons *et al.* (1949) studied the response of schizophrenics to such forms of stress as electro-shock, insulin coma and injection of epinephrine. Blood lymphocytes and polymorphs, haemoglobin, blood glucose and plasma protein were recorded.

Epinephrine was selected for testing pituitary-adrenal functions, because Long (1947) had shown that the administration of epinephrine in animals markedly stimulated adrenal cortical activity, the effect being abolished by hypophysectomy. Dougherty and White (1945) and Long (1947) had previously demonstrated that the lymphocyte response to stress was dependent on an intact pituitary-adrenal-cortical system. Therefore epinephrine would be expected to produce a lymphocytopenia if the pituitary and adrenal glands were functioning normally.

The effect of epinephrine on the circulating lymphocytes in normal and psychotic men was similar, and approximated the effects obtained in psychotics after electro-shock treatment. Insulin also produced a lymphocytopenia, but the changes occurred more slowly and were of longer duration. The findings did not support the view that there is a disorder of pituitary-adrenal function in psychotics, but showed that stimulation of pituitary-adreno-cortical mechanism occurs both in insulin and electro-shock therapy.

Gellhorn and Safford (1948) studied the responsiveness of the sympathetico-adrenal and vagus-insulin systems to anoxia, electroshock and insulin hypoglycaemia. The responsiveness of the centres of the sympathetico-adrenal and vagus-insulin systems, on the basis of blood-sugar determinations, was measured in rats by means of a standard anoxia test, involving five periods of 25 minutes' each exposure at 280 mm. Hg. It was shown that repeated periods of low barometric pressure altered the balance in favour of the sympathetico-adrenal centres. The effects were reversible. Repeated E.C.T. greatly increased the hyperglycaemic response of rats to the standard anoxia test. Repeated insulin comas failed to reproduce the effect of E.C.T., and in fact resulted in a diminished or absent hyperglycaemic response to the anoxia test. Further experiments demonstrated that the low hyperglycaemic response to anoxia after repeated insulin comas was due to the fact that epinephrine now failed to produce glycogenolysis. The results show that E.C.T. increases the reactivity of the sympathetico-adrenal system, and that insulin had no such effect in the experimental animals.

Gershberg and Long (1948) found that insulin hypoglycaemia in rats produced a decrease in adrenal ascorbic acid—an effect known to be due to release of adrenotrophic hormone. They were able to show that the activity of the pituitary was determined by release of epinephrine and not level of blood sugar. The administration of glucose did not prevent the activation of the pituitary in conditions such as exposure to cold or trauma, conditions in which the release of epinephrine is due to causes other than hypoglycaemia.

Meduna (1945) believes that the primary effects of insulin are not the ones responsible for therapeutic success, but that the patients' responses determine the therapeutic result.

The significant responses appear about 30 minutes after the coma dose of insulin has been injected, and constitute the second phase of hypoglycaemic shock. These effects are diametrically opposed to the biological effects of the insulin, e.g., blood-sugar and lactic-acid levels increase and a slight ketosis appears. The total blood fat increases, there is a shift of pH and leucocytosis is present. Similar changes also occur in convulsive therapy, on sympathetico-adrenal stimulation and in diabetes. Meduna finds that some schizophrenics behave like diabetics in Exton Rose Tolerance Tests.

He concludes that a treatment is needed which interferes with the enzyme system of carbohydrate metabolism. This interference must be reversible at will, and must be of a type which will not interrupt the carbohydrate metabolism of the heart or the vital organs.

Solomon (1950) considers that changes in enzyme distribution in the brain produced in insulin coma may be the mechanism of its therapeutic effect.

Meduna and Vaichulis (1948), following up earlier work of Meduna on the existence of an anti-insulinic factor in the blood of schizophrenic patients, carried out experiments with a view to determining the existence of a hyperglycaemic factor in the urine. The authors state that an hyperglycaemic factor isolated from urine of schizophrenics injected intraperitoneally into rabbits produced a significantly greater increase of blood sugar than normal controls. They found that schizophrenics with changes in sensorium, illusions,

confusion, disorientation, etc., are characterized by resistance to insulin and an anti-insulin factor in urine. This disease group is designated as oneirophrenia, and is regarded as having a good prognosis.

Insulin-resistant diabetics also appear to have an anti-insulin factor present in their serum according to Felder (1946).

Proctor *et al.* (1944) found that schizophrenics who improved with insulin or electroshock showed a significant change in oral glucose tolerance test towards the normal. The changes cannot be attributed to insulin or to changes in rate of absorption from gastro-intestinal tract. The pre-treatment glucose tolerance test in this series of schizophrenics seems to show an abnormally prolonged period before the return to fasting levels.

Baruk *et al.* (1942-1945) were able to observe vascular changes in the brain of monkeys and rabbits during hypoglycaemia by direct vision and photography of a cortical field. It was found that there was a depression of the vessels of the brain by a sort of passive aspiration. The brain appeared pale and anaemic during coma, and with recovery from coma the vessels become full and the brain regains colour.

The authors consider that the changes are due to a general collapse of the circulation, and regard the therapeutic effects of insulin as being attributable to changes produced in cerebral circulation.

Sindell (1947) studied the effect of inhalation of amyl nitrite (5 minims) or injection of nicotinic acid (100 mgm.) in 13 patients undergoing insulin coma therapy. Three patients were brought out of coma, and in 9 of the others there was evidence of lightening of coma. The results confirm the view that cerebral vasoconstriction is an important factor in the production of coma with insulin, and suggest that these vasodilator drugs may help in treating irreversible coma.

Baird (1947) found that the insulin given to fasting patients produced a leucocytosis of 15 per cent. in $3\frac{1}{2}$ hours, with a gradual return to normal in 12-15 hours. An absolute lymphocytosis was found by the 3rd hour, and an absolute lymphocytopenia in 6 hours, becoming normal by the 9th hour. The values for red cells, haemoglobin and haematocyte estimation were essentially unchanged.

BIOCHEMISTRY.

Investigations on biochemical changes in blood and nervous tissue have been taken up with renewed vigour, and interesting results have been obtained from studies on carbohydrate and amino-acid metabolism.

Chisler and Himwich (1944) studied the glycogen content of various parts of the central nervous system of dogs subjected to intense hypoglycaemia of varying duration. It was found that decrease in glycogen concentration did not take place in haphazard fashion, but occurred in a definite order which, with the exception of the cerebral cortex, had a rostral to caudal progression. The concentration of the caudate nucleus and corpora quadrigemina decreased first, followed by cortex, thalamus, cerebellum and medulla. The values for the spinal cord were never significantly below the normal.

The order of the changes in glycogen correspond to the progression of symptoms through phases corresponding to phyletic layers of the nervous system described by Himwich (1944) and others. When hypoglycaemia or anoxia is unduly prolonged, the destruction of various cerebral parts occurs in similar sequence.

An investigation into the possible change in glucose metabolism in schizophrenics after a course of insulin shock therapy was carried out by Borenz and Schuster (1949).

It was found that after insulin therapy there was increased tolerance to insulin and epinephrine, i.e., a decreased response to these stimuli, indicating an increased rigidity of homeostasis. The non-glucose-reducing substances in the blood were within normal limits, and remained constant irrespective of changes in glucose produced by insulin or epinephrine. No correlations were found with the insulin tolerance test and the subsequent dose required to produce coma and findings had no prognostic value.

Gottfried and Willner (1949) carried out an extensive series of biochemical investigations on schizophrenics before and after insulin therapy and during the first deep coma. The first series of investigations was designed to determine whether there was adreno-cortical involvement in schizophrenics, and included studies of serum sodium, potassium, magnesium and chlorides. As possible indicators of carbohydrate and lipid metabolism, blood phosphates, total reducing substances, glucose, lactic acid and pyruvic acid were estimated. Possible hepatic dysfunction was studied by cephalin flocculation, thymol turbidity, alkaline phosphatase, and intravenous bromosulphophthalein tests.

The glucose and total reducing substances were sharply reduced during coma. Lactic acid was variable. Pyruvic acid level remained essentially normal. Blood inorganic phosphorus was high in some patients before treatment, but was normal in all after treatment. Inorganic phosphorus of blood and serum dropped during coma. The tests of hepatic function, the bromosulphophthalein sodium tests, the alkaline phosphatase and thymol turbidity test gave normal results before treatment. After treatment the values for thymol turbidity test were increased in a few cases. Results of the cephalin flocculation test were positive. No correlation was found between the abnormal results obtained and the clinical state of the patient.

Weil-Malherbe (1950) states that one of the most constant features of insulin hypoglycaemia is a decrease in the level of inorganic phosphate during the phase of blood-sugar fall, and a gradual return to normal after the blood sugar has reached its lowest value. This is generally attributed to the increased phosphate esterification due to the enhancement of glucose utilization, and is in harmony with the current concept that the function of insulin is primarily that of promoting glucose phosphorylation. In view of the fact that adenosine triphosphate (A.T.P.) has an intimate connection with glucose phosphorylation, Weil-Malherbe decided to study its concentration together with that of calcium in blood during insulin therapy. It was found that the level of inorganic phosphate fell by about 30 per cent. two hours after the injection of insulin and then increased, reaching normal about one hour after termination of coma. The level of A.T.P. remained unchanged two hours after insulin injection, but

increased slightly later. There is a slight fall of serum citrate during the first phase of hypoglycaemia, amounting to 15 per cent. on the average and returning to normal after termination of coma. There was a fall of serum calcium during hypoglycaemia which was quantitatively small but statistically significant. The change in citrate is considered to be related to changes in phosphate and calcium levels rather than to changes in levels of other glucose metabolites.

Billig and Hesser (1944) studied the histamine content of blood of a group of six schizophrenics at various stages of hypoglycaemia during insulin therapy. The depth of coma was assessed according to the clinical stages described by Himwich (1944) and Frostig. It was found that the level of histamine rose as coma deepened. After hypoglycaemia was interrupted by dextrose, the histamine level returned to normal. Ninety per cent. of histamine in blood is carried by leucocytes, particularly eosinophiles. Stimulation or injury to tissue cells causes histamine to escape into the extra-cellular fluid. When the liberation of histamine exceeds the rate of inactivation, the histamine concentration of plasma increases, vascular changes become more pronounced, tissue oedema occurs, and the inactivating capacity of tissues is impaired and histamine level rises with corresponding rapidity.

Ljungberg (1947) finds that blood glutathione is increased during insulin coma and after awakening. The increase varied from 1-44 per cent. He found that all cases showing large increases tended to recover, and that cases with reduced glutathione formation had poor prognosis.

Harris and Harris (1947) find that the amino-acids, leucine and lysine, are decreased during coma in blood of patients undergoing deep insulin treatment. The effect is variable from subject to subject. Glucose also reduced amino acids, though to a lesser extent. They conclude that profound changes in nitrogen metabolism, other than a uniform diffusion of amino acids from blood to tissues, must occur during hypoglycaemic coma.

Glutamic Acid Metabolism.

Quastel and Wheatley (1932) showed that isolated slices of brain tissue are able to use glutamic acid as an oxidizable substrate. They also showed that oxidation was specific for glutamic acid, and none of the other amino acids were able to support respiration of the slices. Normally the brain in life obtains all its energy from the degradation of glucose. However, during certain conditions the brain may use glutamic acid, and Mayer-Gross and Walker (1949) were able to show that small quantities of glutamic acid could restore patients to consciousness. They concluded that the brain metabolized glutamic acid. It is known, however, that the blood brain barrier is highly impermeable to glutamic acid, and it has been shown by Walsh (1949) and verified by Richter and Dawson at Cardiff that when, during intravenous injection, the level in the blood is elevated, the level inside the brain does not increase.

Weil-Malherbe (1949) was able to show that glutamate injection causes a transient liberation of adrenalin into the blood, which in turn causes a rise in blood-sugar level. He concluded therefore that glutamic acid restores consciousness by this mechanism rather than by its use as an oxidizable substrate.

Recent research has provided evidence that the brain does in fact metabolize glutamic acid in hypoglycaemia.

Dawson (1949) estimated glutamic acid and glutamine in rat brain during hypoglycaemia by the microbiological method of Krebs (1948). Post-mortem changes were minimized by liquid air freezing technique. It was found that insulin hypoglycaemia produced a significant decrease in the level of l-glutamic acid in the brain, the extent of which depended on the severity of the hypoglycaemia. At the same time a slight increase in glutamine level in the brain occurred.

It is interesting to note that Stern *et al.* (1949) showed that glucose established an accumulation of glutamic acid in brain cortex slices which had been suspended aerobically in a medium containing l-glutamate, and that Weil-Malherbe (1936) had shown that brain tissue *in vitro* is capable of oxidizing glutamic acid to l-ketoglutaric acid and ammonia, and that the former can then be further oxidized to CO_2 and water.

Krebs and Eggleston (1949) were able to show that l-glutamic acid is effective in preventing the loss of potassium ions from brain cortex slices—a phenomenon associated with the electrical activity of nervous tissue. Nachmansohn *et al.* (1943) also showed that potassium and glutamic acid are necessary for the correct functioning of choline acetylase. Dawson's (1949) work suggests that in hypoglycaemia the brain is able to utilize its glutamic acid reserves. The related investigations being carried out by Richter and Dawson at Cardiff are making fundamental contributions to our knowledge of the functions of nervous tissue during hypoglycaemia.

In conclusion we may say that the reduction of glutamic acid in brain during hypoglycaemia is probably of great physiological importance because glutamic acid activates aerobic oxidation, reactivates choline acetylase and has a specific action in preventing loss of potassium from slices of brain cortex, a process known to be related to electrical activity.

PSYCHOLOGICAL ASPECTS.

Investigations have been carried out on the effect of insulin hypoglycaemia on learning processes and conditioned reflexes.

Riess and Berman (1944) studied the effects of insulin hypoglycaemia on learning processes in rats. Insulin was given in sufficient quantities to produce seizures and lethargy. From maze learning tests it was found that insulin had a greater disintegrative effect on recently learned habits than those of longer establishment. Insulin had a greater disintegrative effect on the learning of a longer and more difficult maze than on a shorter and easier maze. Saline injections were used for control purposes, and found to have no effect on learning. The authors consider that the results give a possible explanation of the mechanism of the production of remission by insulin therapy.

Gellhorn (1946) was able to show that insulin restores inhibited conditioned reflexes.

He was interested in determining whether a positively established conditioned reaction resulting in suppression of a motor action would react

differently to insulin coma from a negatively established motor activity, the latter having been inhibited by lack of reinforcement.

The experiments were performed on 11 rats. In Part A the animal was conditioned to escape in either of two directions on the sound of a bell by means of a simultaneous application of electric shock. When this conditioned reaction had been inhibited through lack of reinforcement insulin coma was applied and degree of recovery of the conditioned response ascertained.

After the response had been fully recovered by reinforcement—Part B consisted of abolishing the conditioned response by application of counter-shock, i.e. at the sound of the bell electric shock was applied to each of the two avenues of escape. When conditioned response of Part A had been completely abolished in this way insulin coma was applied and degree of recovery ascertained. The conditioned reflex was again restored through reinforcement and Part A repeated.

The results show that insulin coma acts on inhibited conditioned reactions and not on positive conditioned reactions regardless of whether they are inhibitory or excitatory in type. It is considered that the restoration of inhibited conditioned reactions is due to heightened hypothalamic activity following insulin coma which reactivates cortical residues of previously established conditioned reactions.

If the action of insulin coma were non-specific the animal could be expected to react to the bell with vigorous escape reaction in both A and B, irrespective of the fundamental differences in the nature of the physiological reactions.

RESULTS.

It is now over 15 years since Sakel introduced the deep insulin treatment of schizophrenia, and its precise value remains a subject of controversy. The reason for this, as Lewis (1945) states, lies in the complexity of psychiatric material. There are many difficulties and obstacles in the way of an attempt to make a scientific assessment of any method of treatment in psychiatry. Discussing these difficulties Rees (1949) considers that they are related to —

1. Provision of satisfactory control groups.
2. The fact that standards and criteria for diagnosis vary among different workers and hospitals, and that as yet we have no satisfactory objective methods of assessing diagnosis or clinical status in psychiatry.
3. The fact that we have no objective methods of measuring recovery, and that varying standards and criteria are used in its assessment by different workers.

Comparison of results obtained by various methods of treatment will be vitiated unless it can be ensured that groups treated by different methods as well as groups used for control purposes are strictly comparable, corresponding not only in age and sex distribution, but also in clinical status and tendency to spontaneous recovery. It is also essential that the assessment or recovery in all groups must be made by the same methods, using identical standards and criteria. These prerequisites for scientific validation make it difficult to combine or compare results from various hospitals because of varying criteria

used in assessing clinical status and recovery, and also possible differences in method and technique of treatment. The fulfilment of these desiderata means that groups should be assessed by the same standards, either by the same worker or by a group of workers, provided it can be shown that they exhibit a high degree of agreement in their ratings.

Finally the follow-up period must be similar in groups, as it has been shown that some patients tend to relapse with the passage of time. It is often impossible to evaluate published results because the authors have not attempted to demonstrate that various groups compared were, in fact, similar in clinical status and prognosis. In some investigations criteria used in assessing recovery are not given, and assessment of recovery may be expressed in various ways from discharge rate to detailed grading based on symptoms and social adaptation.

Penrose (1943-1944) analysed, by an ingenious statistical method, the results of treating 1,600 patients in Ontario mental hospitals by means of insulin therapy or convulsions. Of these, 1,042 were diagnosed "schizophrenia," and it was found that the remission rate attributable to shock therapy was negligible for the schizophrenics and the convulsant treatment was more effective than insulin. Although the investigation was of a high statistical standard, it is difficult to accept the results as the final verdict, as the patients were collected from various hospitals and therefore diagnosed by different workers. Information is inadequate on the technique of treatment and on factors of prognostic significance in treated and control groups.

A comprehensive survey has been published by a Temporary Commission on State Hospital Problems in New York on Insulin Therapy. A group of 1,228 schizophrenics were compared with a comparable non-treated group of 876 patients. 79.5 per cent. of insulin-treated patients were able to leave hospital against 58.8 per cent. in the control group. The period of hospitalization was 3.8 months shorter in the treated group.

Freudenberg (1947) in a careful review of 10 years' experience on insulin therapy at Moorcroft House, London, found that amongst the cases with a duration of under one year 80.1 per cent. were able to leave hospital, and of patients with an illness of 1-3 years' duration 53.6 per cent. were able to return to the community. If the illness was over three years' duration before treatment, 28.6 per cent. could be discharged.

Mayer-Gross (1947) compared the results of deep insulin therapy in 50 early schizophrenics, ill one year or less, and treated with insulin at the Crichton Royal Hospital with 188 schizophrenics of the same duration receiving routine hospital care. The control group was of relatively good prognosis, and any method giving better results than this would have much to say in its favour. 54 per cent. of the insulin group had total or social recovery, compared with 34 per cent. of the control group.

It has been stated that insulin therapy, though effecting an immediate improvement, tends to give a greater number of relapses. Comparison of the two groups in this respect, however, showed no significant differences.

Finiefs (1948) reviewed the results of treatment of a thousand cases of schizophrenia at the Three Counties Hospital, Arlesey. Of the total of 1,009

cases, 563 had insulin and convulsion therapy while 446 received no special treatment. 54.2 per cent. of the insulin-treated group made total or social recoveries, compared with 34.5 per cent. of patients receiving hospital care without special physical methods. The average stay in hospital was 5.2 months, compared with 8.3 months in control group.

Dedichen (1946) compared 1,459 shock-treated and 969 patients receiving routine hospital care in 17 Norwegian hospitals. According to his figures the immediate results in schizophrenia of less than 1 year's duration are 4-5 times as good as untreated controls.

Hinko and Lipschutz (1947) reviewed results of shock treatment (insulin, metrazol and E.C.T.) in 457 patients, in comparison with a control group of 289 patients receiving routine hospital care, matched for age, sex and diagnosis. The results assessed in terms of parole were insulin 53.4 per cent., metrazol 37.6 per cent., electroshock 45.8 per cent., control group 35.6 per cent. The percentage of patients on parole after 5 years was slightly higher for the treated than for the control group. It was found that if treatment was given during the first year of hospital residence, a saving of 422 hospital days per patient is obtained, and that remission permitting parole occurs in one-third the time required for spontaneous remission. The practical implications of this in terms of bed capacity for treatable patients are obvious.

The authors conclude that insulin is more effective than E.C.T. in schizophrenia, particularly in catatonic and paranoid types.

Bond and Rivers (1944) compared the results obtaining in a control group of 100 unselected schizophrenics admitted before the advent of shock therapies with a group of 251 schizophrenics treated by insulin coma therapy. In the control group 16 per cent. recovered or much improved at end of hospital stay, 16 per cent. recovered or much improved at end of 5 years, and 14 per cent. recovered or much improved at end of 6-7 years.

In the insulin-treated group 54 per cent. recovered or much improved with treatment; 49 were followed up for 5 years; of these, 41 per cent. maintained their status compared with 16 per cent. of control group.

Cossa and Lombard (1948) compared the results by Sakel's treatment between 1938 and 1944 in 100 schizophrenics with 82 schizophrenics treated since. 43.7 per cent. of the former group had a complete remission compared with 28 per cent. in the latter group. The author concludes that the insulin of 1948 is not the same as that of 1939. This surprising conclusion can hardly be accepted unless it can be shown that both groups were identical in clinical status and prognosis, and were treated equally adequately and assessed in precisely the same way. (See also p. 645).

Gralnick (1945), in a seven-year survey of insulin treatment of 554 cases of schizophrenia, concludes that if the treatment is given early enough remissions occur earlier, are of better quality, and are more stable than spontaneous remissions. Insulin gives better results than electro-convulsive therapy, and the author recommends more discrimination in the use of electro-convulsive therapy in schizophrenics. Gralnick claims that insulin treatment has worthwhile results in cases of schizophrenia of 1, 2 and even 3 years' duration, regardless of age and type. 73 per cent. of patients paroled 6 years returned

to hospital. It is stated that good remission may occur with as few as 15-20 treatments, and few if any comas.

Gralnick (1946) in a 3-year survey of the comparative value of electro-shock and insulin therapy concludes that insulin coma therapy is the method of choice for schizophrenia. The important thing is an improved method of selecting patients for shock therapies.

Goldfarb *et al.* (1946) described results of treatment of psychoses in military personnel overseas who had not experienced active combat. The schizophrenics were of various types, some atypical. The results with insulin coma therapy were as follows: Complete remission 33 per cent., improved 44 per cent., not improved 23 per cent., and for electro-convulsive therapy 25 per cent. complete remission, 54 per cent. improved and 21 per cent. not improved. No significant differences were noted in the rates for various types of schizophrenia.

Bond and Shurley (1946) with technique of producing early induction of deeper, longer comas investigated the results obtained in a group of 309 schizophrenics treated in a 10-year period: 48.8 per cent. recovered or were much improved at the end of treatment; the figure was 47 per cent. at the end of the first year, and 37 per cent. at the end of 5 years.

In patients with less than 18 months' duration of illness 63 per cent. were recovered or much improved after treatment, and in 39 per cent. the improvement was well maintained, the results being at least twice as good as their controls.

Niver and Catlin (1947) described treatment of 135 soldiers who developed psychosis after extensive military service. Best results were found with insulin treatment combined with occasional convulsive treatment and a final course of convulsive treatment. 56.4 per cent. of the group were able to leave hospital, 21.8 per cent. to family care, and 21.8 per cent. transferred to veterans' hospital.

Garmany (1946) studied two groups of 100 schizophrenics diagnosed as such during their service in the Navy. Applying a high standard of recovery, including restoration of a lively but restrained affect, realization of having been ill, spontaneity, an ability to foresee and plan the future, it was found that the results were overwhelmingly in favour of insulin therapy, with 56 per cent. recovery compared with 2 per cent. in the control group.

Chapuis and Georgi (1945) investigated the results of insulin therapy on 81 schizophrenics followed up for 5-7 years. By combining insulin shock with cardiazol they obtained 52.2 per cent. remissions, and over half had no recurrence for 3-7 years.

Weil and Moriarty (1944) report improvement in 15 of 20 patients treated with insulin after failure with electro-shock, and worth-while improvement in over half the cases with poor prognosis and long-standing psychotic symptoms.

Feldman *et al.* (1947) report that 66 per cent. of schizophrenics treated with insulin coma therapy went home, but there was a high readmission rate, and in general these people continued to be social and economic problems.

Paster and Holtzman (1949) studied the results obtained in a group of

1,000 psychiatric veterans treated by electro-convulsive therapy and insulin. They found that insulin was more effective than electro-shock in the treatment of catatonic and paranoid schizophrenia, and the remissions with insulin were more lasting.

Rees (1949) described a comparative study of the treatment results in a group of 160 schizophrenics by electronarcosis, insulin coma therapy and electroshock therapy. An item sheet of some 300 items was completed for each patient, and the information transcribed to punched cards and analysed by a Hollerith machine. The groups were matched for age, sex and various prognostic factors. The immediate results were as follows. Full recovery: electronarcosis 8 per cent., insulin coma 29 per cent., and electroshock 8 per cent.; improved and discharged: electronarcosis 23 per cent., insulin coma 30 per cent., and electroshock 24 per cent.

The higher proportion of recoveries with insulin therapy is statistically significant. The relapse rate was high in electronarcosis and electroshock therapy groups, and relapse occurred sooner than in insulin-treated group. With insulin therapy only 7 per cent. of the recovered group relapsed, compared with 38 per cent. in the improved group. On follow-up investigations extending over a period of 3 years, 27 per cent. of insulin group remained fully recovered, compared with 5 per cent. in electronarcosis group and 2 per cent. of electroshock group.

Matching the groups accurately for prognostic factors further enhanced the results obtained by insulin compared with electronarcosis and electroshock therapy. Compared with groups treated with routine hospital care only, insulin therapy was the only method giving significantly better results. The author concluded that insulin therapy was far superior to electronarcosis and electroshock in the treatment of schizophrenia, and was the only method giving better results than the control groups.

The better quality of improvement obtained with insulin therapy compared with that occurring spontaneously has been stressed by Finiefs (1948), Mayer-Gross (1947), Freudenberg (1947), and many other authors.

PROGNOSIS.

A number of clinical features have been found to be related to the outcome of insulin coma treatment in schizophrenia.

Freudenberg (1947) finds that atypical cases characterized by admixture of manic-depressive and confusional features do best, then catatonics and paranoids, whereas hebephrenics do less well. An acute onset is more favourable than an insidious onset. He considers that duration of illness is the most important prognostic factor. Patients with good previous personality will, with interests and good contact with reality, tend to be associated with a favourable outcome.

Bond and Shurley (1946) find prognosis poor in patients less than 16 years of age and cases with long duration of illness. If treatment is given during the first 18 months the outlook is better. They did not find that prepsychotic personality was related to outcome.

Meduna and McCulloch differentiate true from pseudo-schizophrenia, and suggest for the latter the new term "oneirophrenia." This type is characterized by an acute onset, sometimes associated with alteration of body temperature and leucocytosis. Defective judgment, affective disturbance and clouding of consciousness are usually present. They consider that there is evidence of disturbed carbohydrate metabolism in this condition, and that this is the type with favourable prognosis with insulin coma therapy.

Smith (1947) finds cases with well-marked thought disorder in clear consciousness, with little emotional disturbance, respond poorly.

Rees (1949) found that tendency to recover is associated with the following features: Stable previous personality, broad interests, an illness of less than 1 year's duration and of sudden onset. The presence of exogenic factors, affective admixture and positive family history also occurred in higher proportion in the recovered patients. Failure to improve with treatment was associated with a clear predisposition to mental illness, very unstable personality, schizoid in type, narrow interests and a gradual onset of illness.

The importance of duration of illness in prognosis is also stressed by Sargant (1949), Chapuis and Georgi (1945), Bond and Shurley (1946), Hinko and Lipschutz (1947), Dedichen (1948).

Ljungberg (1947) found that patients showing little increase in blood glutathione during insulin coma have a poor prognosis, whereas cases with moderate increases (in the region of 5 per cent.) tended to improve, but not to the extent of full recovery, and those with large increases (18-44 per cent.) tended to recover.

The foregoing reports support previous findings that duration of illness, atypicality, sudden onset and previous personality are clinical features of prognostic importance.

CONCLUSIONS.

During the period under review further modifications in technique have been described. For the treatment of schizophrenia the available evidence suggests that a certain minimum number of comas of sufficient depth and duration are required for therapeutic success. It is very doubtful indeed whether subshock insulin therapy has any real value in the treatment of schizophrenia, but when used as part of a psychotherapeutic programme, it has been found valuable in the treatment of certain neuroses and psychosomatic disorders. Convulsive therapy in combination with insulin coma therapy has been found useful when affective features were present, and in helping to overcome insulin resistance. Convulsive therapy alone is of very doubtful value in the treatment of schizophrenia, and there is conclusive evidence that it is far less effective in the treatment of schizophrenia than deep insulin therapy. Other therapeutic techniques advocated for use with insulin therapy are described, but as yet their therapeutic value cannot be finally assessed.

Interesting findings in physiological, biochemical and psychological aspects of insulin therapy are discussed, and certain biochemical investigations relating to the metabolism of glutamic acid and other amino acids is promising.

The complexity of psychiatric material and the difficulty of establishing satisfactory controls are some of the reasons why the estimation of the therapeutic value of insulin coma therapy in schizophrenia has been so long delayed. From the results of strictly controlled investigations we now have strong evidence that insulin coma therapy produces significantly better results than obtained by routine hospital care. Furthermore, the remission occurs earlier, is of better quality and is more lasting. Incomplete recoveries tend to relapse early, whereas complete recoveries tend to remain well.

There is a consensus of opinion that duration of illness is one of the most important factors relating to outcome of treatment. Other clinical features which may influence the prognosis are discussed.

Follow-up studies show that the discrepancy between the results of treated and control series diminishes with time, but remains significantly to the advantage of the insulin-treated patients.

It may be concluded that while insulin coma therapy cannot be regarded as a specific treatment for schizophrenia, its therapeutic results should stimulate further research into the nature of the underlying changes responsible for recovery as well as those responsible for relapse after improvement, with a view to discovering a specific remedy for schizophrenia.

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THE NEUROSURGICAL TREATMENT OF MENTAL ILLNESS.

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It has proved a difficult matter to keep pace with the spate of papers published on leucotomy or lobotomy and its various modifications, particularly during the last two years. A selection has had to be made from the considerable number of papers in the bibliography. The most spectacular publication is the large volume entitled *Selective Partial Ablation of the Frontal Cortex*, from the Columbia-Greystone Associates and edited by Mettler and published in 1949. This is a truly immense piece of work carried out by a team of distinguished workers, and covering 500 pages. It is quite impossible to summarize this publication in a short review, and the original should be read! In addition the Anglo-American Symposium at the Royal Society of Medicine arranged by Sargant should be read.

Birch (1947) describes an interesting occurrence in World War I. In 1915, at Suvla Bay, a man was brought to him who had had a rifle bullet through his frontal lobes, from one temple to the other. The man walked aboard the hospital ship as if nothing had happened to him. Although he appeared to be quite normal mentally, his friends all thought that he had become a much more cheerful person. He was under observation for two weeks and remained quite well, but was then unfortunately lost sight of. This is an interesting sidelight on leucotomy.

ANATOMICAL AND PATHOLOGICAL CONSIDERATIONS.

Sheps (1945), in his study of the nuclear structure and connections of the human thalamus, based on three cases of thalamic degeneration following cortical destruction, states that there was in the thalamus,

(a) Complete degeneration of—

- (I) the nuclei anteroventralis and anteromedialis ;
- (II) the internal small-celled portion of the dorsomedial nucleus ;
- (III) the nucleus ventralis anterior ;
- (IV) the pulvinar ;
- (V) the nuclei lateralis dorsalis and lateralis posterior.

(b) Although the centrum medianum and the reticular nucleus showed no appreciable reduction of neurones, there was a gliosis secondary to the degeneration of the fibres of passage.

(c) The nuclei ventralis lateralis and ventralis posterior showed a falling out of the small neurones, but the large neurones were preserved. The nucleus submedius showed some reduction of neurones.

The magnocellular part of the dorsomedial nucleus is intimately connected with the nucleus paracentralis and the nucleus centralis lateralis. The increase in size of the dorsomedial nucleus in man appears to be related to increase of the frontal granular cortex.

Mettler (1947), in a long discussion of the projection from the frontal areas in the primate cerebral cortex, states that area 9 projects on to the septal nuclei, and is the principal frontal locus which sends fibres to the caudate nucleus via the subcallosal fasciculus. In the thalamus he points out that it projects on the medial nucleus which sends fibres to areas 12 to 8, the ventral part of the lateral group of the thalamic nuclei which sends fibres to areas 4 and 6, and the ventral nucleus of this part of the lateral group which sends fibres to an undetermined cortical locus. He found that bilateral removal of area 10 did not produce any definite abnormalities in behaviour, but that removal of area 9 did. There was mild spontaneous overactivity with inadequate relaxation of the musculature, but no definite resistance to passive movement. He points out that it is theoretically possible for area 9 to influence the autonomic system by virtue of the cortico-septal pathway, but that stimulation or ablation of area 9 produces surprisingly few autonomic effects.

Toncray and Krieg (1946) give a very good account of the comparative anatomy of the human thalamic nuclei. The nucleus medialis of man is well described and illustrated. It is, of course, one of the largest nuclei of the thalamus and, from our point of view, one of the most important. It is surrounded on all but its medial side by the internal lamina. The authors point out that the nucleus medialis, nucleus ventralis lateralis and pulvinar are believed to increase in size, due to their connection with the increasing frontal area, cerebellum and inferior parietal and occipital association areas. From a phylogenetic point of view there is a rapid development of the lateral thalamus, due to the great expansion of the association areas of the cerebrum.

Glees (1948) studied the results of leucotomy in apes. He found degeneration of ascending fibres in layers 3 and 4 of the frontal lobes. The orbital region of the frontal lobes was connected with the medial part of the medial thalamic nucleus, the dorsal region of the frontal lobes with the lateral portion of the medial thalamic nucleus. Fibres from the hypothalamus probably end in the medial nucleus of the thalamus.

Lashley (1944) found in rats that severing transcortical connections in the rat failed to cause any deterioration in maze performance, and when deterioration did occur, it was due to the interruption of thalamo-cortical fibres or to the destruction of cortical tissue.

Messimy (1948) found bilateral prefrontal excision in animals caused changes in character, extrapyramidal hypertony and neurovegetative disturbances. He considers the role of the prefrontal cortex to be an inhibitory action on the extra-pyramidal system via the fronto-thalamic connections. Moss and Harlow (1948) found that after prefrontal lobotomy and extensive unilateral decortication of three macaque monkeys, one showed no impairment whatsoever of discrimination learning, discrimination-reversal learning and delayed reaction. The other two solved the problems within the range but below the mean of performance of normal monkeys. Mettler (1947) found removal of areas 9 and 10 caused degeneration in the medial nucleus of the thalamus. He prepared a map of the thalamus with the projection areas from the cortex marked on it.

Ward and McCulloch (1947) found that the paraventricular nuclei of the hypothalamus receive projections from area 46 and from the orbital surface. Area 10 is connected to the posterior portion of the periventricular nucleus, the path running in the dorsal longitudinal fasciculus.

Meyer and McLardy (1947) report on 27 cases of leucotomy. In only a few was the aim attained of a bilateral lesion through the whole of the white matter. "In several cases the damage to the prefrontal region was negligible." They see a possible correlation between improvement of depressive symptoms and orbital involvement.

Meyer and Beck (1945) point out that the plane of the cut varies enormously, and show the different plane in 9 cases sent to them for examination.

M. Meyer (1949) examined brains from patients who had survived a short time after leucotomy. She found that when the leucotomy extended into the white matter underlying the dysgranular and agranular frontal cortex, terminal degeneration was present in the mammillary body, the dorsomedial and ventrolateral group of thalamic nuclei, the globus pallidus, zona incerta, Forel's field, the red nucleus and the subthalamic nucleus. The cortical fields projecting to these centres are confined to the rostral part of Brodmann's areas 6, 8, and posterior 9. There was no evidence of a projection from the rostral cingular gyrus to the anterior nucleus of the thalamus. A direct cortico-pallidal pathway is very interesting.

Freeman and Watts (1947), in one case examined 20 months after leucotomy, found retrograde degeneration in the thalamus, chiefly in the lateral portion of the medial nucleus, but also in the antero-medial portion of the nucleus ventralis lateralis and in the neighbouring nucleus anterior, especially on the left side. The nucleus submedius was also affected. In a second case, examined 4 months after leucotomy, in addition to the usual degeneration, there was degeneration of the anterior and medial portions of the medial nucleus on the left side. In a third case, 4 years after one operation and 2 years after the second, there was degeneration of the lateral portion of the medial nucleus and a large part of the nucleus ventralis lateralis and nucleus ventralis anterior. In a fourth case, 4 months after operation, there was degeneration of the lateral portion of the medial nucleus and also relatively complete degeneration of all except the medial portion of the anterior nucleus. The nucleus ventralis lateralis was severely affected in its anterior portion, and the nucleus ventralis anterior almost completely. The nucleus lateralis was degenerated in its antero-dorsal aspect. From the results in these and 8 other cases, the authors conclude that the central part of the medial nucleus of the thalamus projects to the frontal pole, the lateral portion to the convexity, the medial portion to the base. The anterior nucleus projects to the medial surface of the hemisphere. The medial nucleus can be regarded as the anatomic substrate for emotional experience, especially for ideational processes relating to the self. The same authors (1947), after examining the brains of 4 patients operated on some months before by leucotomy, found that it was possible to indicate areas in the thalamic nuclei which correspond closely with areas of the cortex. The central part of the median nucleus of the thalamus projects to areas 9, 10 and 11 of the frontal pole, the lateral part to the convexity

of the frontal pole, and the median part to the base. The anterior nucleus projects to the medial surface of the hemisphere, while the lateral group of nuclei project to the motor and premotor areas.

Greenwood (1948) reports on a brain of a patient who died from coronary thrombosis $4\frac{1}{2}$ months after leucotomy. There was no atrophy of the frontal poles. The dorsal medial nucleus had undergone extensive degeneration on both sides, characterized by reduction in the number of ganglion cells. There was proliferation of the glia, occasional shadow cells, and occasional indications of neuronophagia. The surgical lesions on both sides entered the ventricle, but without damaging the caudate nucleus.

Norman (1945), in a case of bilateral premotor frontal lobe atrophy of the Strümpell type, found severe retrograde degeneration of the whole of the dorso-medial nucleus of the thalamus.

E.E.G. FINDINGS.

Davis (1941) found that apart from some increase in instability there was no significant change in the E.E.G. in the frontal area which had been undercut.

Cohn (1945) found that prefrontal leucotomy produced focal slow waves which may or may not persist. The return to a normal pattern requires from 1-3 months. Some patients show an apparently normal early recovery, and then again exhibit grossly abnormal variations in potential in the region of the original injury. Hyperventilation after cerebral injury produced slow wave activity in brains that before injury were uninfluenced by this.

Greville and Last (1946), in a series of 35 cases, found that the voltage of the alpha rhythm tends to increase after the operation, whilst the voltage of the fast activity tends to decrease. Delta activity appeared in about 57 per cent. of the cases, and was just as common in the above 35-year age group as in the below 35. It appeared to arise in the prefrontal areas. Theta activity was widespread, occurring in about 60 per cent. of cases and tending to diminish with time.

Stevens and Mosovich (1947) found in a group of 24 patients examined 6 months to 8 years after operation definite abnormalities over the frontal region in 23 out of the 24 patients. Twenty-one showed high-voltage delta waves of 3-7 per second over the frontal region. Only 9 of the 24 had normal alpha activity; the rest of the records included 5 with a low-voltage, rapid, irregular pattern, and 10 with diffusely abnormal and disorganized tracings. There was no correlation between post-operative behaviour and E.E.G. abnormality. The delta waves from the frontal areas may be due to focal damage to cortical cells, secondary atrophy of the frontal cortex, irritation of residual lipiodol, or the release of subcortical centres due to transection of the anterior thalamic peduncle.

Stevens (1948) found of 9 schizophrenics that all showed an abnormal E.E.G., characterized by high-voltage 3-7 per second waves over the frontal region bilaterally. There was no correlation between post-operative behaviour and E.E.G. abnormality.

Poppen *et al.* (1948) found that patients who had no post-operative convulsions showed abnormal E.E.G. patterns in 20 per cent. before operation, and 50 per cent. post-operatively, with a gradual return to the pre-operative level. Of those with post-operative convulsions, 50 per cent. had abnormal pre-operative patterns, and 65 per cent. post-operative.

Lennox and Coolidge (1949) found after leucotomy a generalized slowing, most prominent in the frontal leads in the first few days. This slowly improved. The long-term residue was a $\frac{1}{2}$ -1 per second baseline sway with normal frequencies superimposed. The 12-per-second waves, which occur during sleep before leucotomy in anterior leads, practically disappear afterwards, due, it is assumed, to degeneration of the nucleus centralis medialis of the thalamus. The 14-15-per-second waves occurring during sleep, and which are more frequent in central leads and less frequent in frontal leads after leucotomy, are presumed to originate in the nucleus centralis lateralis of the thalamus.

INDICATIONS AND CONTRA-INDICATIONS.

Cook (1946) divides his candidates for treatment into four categories:

(a) Depressives with severe agitation, etc., in which E.C.T. has failed or is contra-indicated.

(b) Obsessive-compulsive states.

(c) Florid schizophrenic reactions.

(d) Long-standing violent conduct disturbances with increased mental tension, mainly in catatonics, but also in some aggressive psychopaths, epileptics, encephalitics and mental defectives.

Out of 48 cases operated on, 19 remitted or recovered, 8 were greatly improved and 10 showed some improvement of conduct. He thinks that patients who remain well for 18 months may regard themselves as permanently cured. There was a distinct rarity of frontal lobe injury symptoms.

Peters (1947) reports on 71 hopeless schizophrenics of long duration. The pre-leucotomy traits which were considered to be favourable indications for operation, were based on two principles: (1) heightened activity, (2) integrity and dominance of cortical centres remaining. The following traits are based on (1) energy, activity, restlessness and agitation, and on (2) mood stability, purposiveness, initiative, evident interests, grasp of reality, absence of hallucinations, aggressiveness and flight of ideas.

Poppen *et al.* (1948) consider the indications for lobotomy, in the order of good results obtained in a series of 470 patients, to be: involuntal melancholia, agitated depression, severe obsessive-compulsive states, paranoid and catatonic dementia praecox. There is relief of tension, self-concern, fear and depression. Perverts, kleptomaniacs and criminals who are not concerned about their misdeeds are not relieved.

Kalinowsky and Scarff (1948) very rightly point out that the physician's first care is for the good of the patient; the relatives' likes and dislikes, comforts and discomforts must take second place. A patient who has a pleasant, well-adjusted personality should not present post-operative difficulty. They request a minimum sojourn of two months in hospital. The operation should

always, if possible, be carried out before the patient has become deteriorated. The authors used E.C.T. as a test for suitable cases of schizophrenia for leucotomy. If the patient showed some improvement after 4-5 shocks, then he was considered suitable for leucotomy. Hebephrenics should usually be rejected. Catatonics are good subjects. Paranoid schizophrenics give the best results. Severe hypochondriacs give good results. Neurotics who do not benefit from psychotherapy should be accepted for operation, but psychopathic personalities as a rule do not improve—once a liar, always a liar!

Frank (1946a) considers, from a consideration of 200 cases that leucotomy is contra-indicated in patients with a shallow affect, with an organic senile syndrome; a blood urea of over 50 mgm. per cent. is an absolute contra-indication. If the clinical signs are indefinite, then the state of the retinal vessels, an organic Rorschach and discrepancy of the verbal to the disadvantage of performance intelligence test scores are of great value.

Frank (1946b) considers cerebral deterioration from arteriosclerosis or senility as a contra-indication. Kraus (1947) thinks that treatment by occupational therapy renders leucotomy superfluous. Dublineau *et al.* (1947) report a case of a severe obsessional of many years' standing treated by leucotomy. Shorvon (1947) found in 5 cases of depersonalization that leucotomy gave good results in all. Thorpe (1946) described the effects in 2 cases of post-encephalitic conduct disorders. In both cases the impulsiveness and irritability were relieved, but they were both irresponsible.

Schwarz (1945) describes a case of depression with post-encephalitic Parkinsonism predominating on the left side, treated by unilateral (right) leucotomy. The patient's attitude towards his illness changed and there was undoubted improvement in his Parkinsonian symptoms.

Delay *et al.* (1948) found, in a case of epilepsy with non-systematic delusional ideas, confusion and alteration of character, that frontal lobectomy removed the delusional ideas completely. Mental deterioration appeared slowly. Turnbull and Davidson (1949), in a series of 100 cases, found seizures in 3 per cent. of cases. A small group of psychoneurotics and involutional melancholics which had not responded to a long course of treatment did very well with leucotomy. Stevens (1948) found, in his series of 30 cases, 10 who developed seizures; 6 of these had had E.C.T. prior to leucotomy, and only 3 of the group of 20 without seizures. Pool (1949), in his series of 52 cases of topectomy had 14 per cent. of seizures.

Mackay (1948) found, in a group of 20 cases of psychopathic feeble-minded patients, that there was marked improvement in some 50 per cent. of cases. Five of the cases were discharged and two more were about to be. Klein and Tardieu (1949) recommend leucotomy for idiots who show a continual state of agitation. The leucotomy is stated to abolish the agitation.

Engler (1948) found disappointing results in mental defectives of varying degree of defect, and considers that the operation is contra-indicated for the cure of behaviour problems in mental defectives because (a) the mortality is high, (b) the operation may be difficult to perform on the malformed brain of mental defectives, (c) the percentage of improvement is minimal, (d) epilepsy is likely to be increased or induced, and (e) the percentage of further deteriora-

tion is likely to be high. He wisely points out that a person whose I.Q. is only 30-50 cannot afford to lose the small amount of I.Q. that a person with an I.Q. of 90-100 can lose without its being apparent.

Solomon (1949) sums up the pros and cons of leucotomy very well. He says :

1. Tension, apprehension, fear, concern, worry and agitation are greatly reduced or abolished.

2. Excitement, aggressive and assaultive behaviour, emotional outbursts and rage-like exhibitions, although not infrequently intensified shortly after the operation, tend to diminish and disappear within a few weeks or months.

3. Paranoid ideas tend to lessen to the vanishing point or, if continued in an attenuated form, cease to lead to overt expressions.

4. Obsessive thinking becomes less distracting, compulsive actions no longer occur and ritualistic behaviour ceases.

5. Long-standing hallucinations may lessen or may lead to a lessened response ; only rarely do they disappear entirely.

6. Anergic states are occasionally transformed into states of greater activity, but frequently are unchanged or activity may even be reduced.

RELIEF OF PAIN.

Freeman and Watts (1946) describe 5 cases of intractable pain operated on by prefrontal leucotomy with success. Recurrent carcinoma, tabes, thalamic syndrome, cauda equina injury, hysterical contractures and a phantom limb all derived benefit.

Poppen (1947) describes a case with severe pain in the left side of the face, that would not respond to any form of treatment, including section of the fifth nerve. Two years ago a section of the fronto-thalamic tract was made. The patient is now working in a job, happy and without any vestige of pain.

Freeman and Watts (1948) consider that lobotomy does not interfere with the perception of pain, but rather with its evaluation, apparently by eliminating the emotional component which arises in the thalamus.

Sweet (1947), after discussing the use of chordotomy or tractotomy in the relief of pain, discusses the use of prefrontal lobotomy to relieve the pain of malignant disease. He reports relief of phantom limb pain in one patient after partial post-central girectomy.

Watts and Freeman (1948) have used with considerable success leucotomy in the treatment of intractable pain due to carcinoma, tabes dorsalis, radiculitis, causalgia, phantom limb and the thalamic syndrome. The patients still feel the pain but are no longer concerned with the affective element, and are relieved from the fear of it. Poppen *et al.* (1948) consider that patients with intractable pain lose all fear of pain or death after leucotomy.

Le Beau *et al.* (1948) performed prefrontal topectomy for the relief of pain in 10 cases ; in 5 the pain was of organic origin, 3 were cases of anaesthesia dolorosa and 2 of chronic neuralgia in hypochondriacs. In 8 cases the location

of the pain was cranial or facial. In 8 cases the pain disappeared, and in the other 2 the results were mediocre. Four of the 8 said they had no more pain; 3 never complained spontaneously and slept well. The authors consider that areas 9 and 10 are believed to form part of a bilateral symmetrical circuit including the median and lateral nuclei of the thalamus and the septal nuclei, within which the conscious integration of pain see is to take place.

Williams (1949) found unilateral lobotomy unsuccessful in one case of contralateral post-herpetic neuralgia. Stender (1948) found, in 2 cases of unilateral intractable pain, that a unilateral prefrontal lobotomy led to complete freedom from pain, and not merely to decreased affective reaction to pain still perceived. Puech (1949) treated 5 cases by operation either on the median dorsal nucleus for mental disturbances, or on the external nucleus for pain. Riechert (1949) performed leucotomy on 6 cases for intractable pain, 2 of them due to progressive syringomyelia. Although the pain persisted, the patients' emotional reaction changed completely. Three conditions are considered necessary before leucotomy is performed for the relief of pain: (1) the presence of severe chronic pain responding only to morphine; (2) failure of other operations or contra-indications to surgical intervention on the grounds of age or general health; (3) the patient and his family must be informed of subsequent personality changes.

Wertheimer and Lecuire (1949) found the violent phantom pain, after a partial amputation of the left leg, disappear as a result of parietal gyrectomy in a man of 58. Scott and Wycis (1949) recommend cerebral surgery in preference to section of the fifth and ninth cranial nerves, etc., if alcohol injection of the fifth nerve does not relieve pain in nasopharyngeal malignant disease. Chapman (1949) found that leucotomy patients were oversensitive to painful stimuli of the skin after operation. There was much less tolerance of heat-stimuli, the patients after leucotomy winced and withdrew their head at significantly less intense heat stimulation than they did before leucotomy.

Scarff (1949) operated on one side only in 33 patients, the majority with neoplasms. His results were not as satisfactory as those reported by other authors with bilateral operation. There was evidence that an ipsilateral leucotomy was more effective if the pain was localized to one side of the body.

Dynes and Poppen (1949) found, in a series of 18 cases with intractable pain, that the pain of metastatic malignant disease was most readily relieved. They noted two main effects: firstly, that there was an alteration of the pain pattern, or the patient's appreciation of pain, and secondly, that the patient no longer worried about the problems of living, or the pain and distress of dying. These authors take a very conservative view in the selection of cases. They do not like unilateral operation.

It is doubtful whether the actual pain is removed or, as Freeman says, "just disappears." It is much more likely that it is the unpleasantness of the pain that disappears—the affective side in other words. Koskoff (1949) suggests that the operation for the relief of pain is really for the relief of suffering.

Scarff (1948a) reported 3 cases which indicate that unilateral prefrontal lobotomy will relieve ipsilateral, contralateral and bilateral pain. Symptoms

commonly associated with the withdrawal of morphine from patients previously heavily addicted to its use because of pain did not occur following unilateral prefrontal lobotomy.

SURGICAL DEVELOPMENTS AND TECHNIQUE.

During the period under review the neurosurgeons have been working hard developing new methods of approach, varying the amount of brain destroyed, attacking either the grey matter or the white, penetrating to the thalamus, and even trying to do a leucotomy without the use of the knife at all, by supersonic waves.

Lynn and Putnam (1943) report attempts to destroy areas of brain by means of focused supersonic waves. They succeeded in producing *in vivo* lesions of the brain and cord in living animals, but there was injury and necrosis of the overlying soft tissues, i.e. there is damage to all the tissues in the path of the beam acting for 10–15 minutes. The area of damage shows a coagulation necrosis, and is somewhat similar to that caused by high explosives. In this country work has been carried out at the Burden Neurological Institute at Bristol by Golla and Grey Walter trying to focus supersonic waves, but so far it has proved impossible to avoid damaging the superficial structures.

Uihlein and Love (1948) describe a localizer for providing points of reference for the incision into the brain. A roentgenogram is taken with the localizer applied to the scalp.

Stjernberg (1947) reports the result of pneumo-encephalographic examination on 13 female cases which had shown no or slow improvement. The examinations were made at least one year after operation. He found cerebral atrophy of varying degree in all, but in no case of high degree. Four cases showed porencephalous cavities. There was no connection between degree of atrophy and clinical result. Broager (1947) preferably operates only on patients who have been encephalographed, placing the burr-holes so that the frontal incision in the white matter is just in front of the anterior horns. If the bone is too thick, the opening is enlarged with forceps—this was done in half his cases. This author has considered trepanning and replacing the bone disc as a routine procedure.

Barreto (1945) reports his results in 42 chronic cases, all of whom had had metrazol, insulin and even Moniz leucotomy. This worker has a pneumo-encephalography done before operation so that the ventricles may easily be localized. He has devised a leucotome which, in addition to cutting the white matter, leaves iodized-oil in its track.

Reitman (1946) described results in 22 patients in which the orbital cortex was partly isolated. The fibres severed probably included the thalamo-cortical radiation to areas 10, 11, 12 and part of 46. The greater part of the orbital cortex would be isolated. The symptoms produced by the operation were extraversion, increased motor activity and euphoria.

Hofstatter *et al.* (1945) report results from 22 old-standing chronic schizophrenics of 3½ years' average duration, who had a bilateral lower quadrant leucotomy only. They found a recovery rate of 40 per cent. The incidence of urinary incontinence was stated to be lower. There were no deaths, and

no cases of epilepsy. The authors consider that the basal part of the frontal lobes plays an important part in the regulation of emotion.

Amaral and Parado Leitao (1948) found 72 per cent. improvement in 36 psychotic patients. They recommend Moniz' operation for early cases, and the more extensive operation of Freeman for unsuccessful and more advanced cases.

Lewis, A. (1946) points out how great are the variations in the cut, and that some of the anatomical changes which follow may be due to section of fibres running from the orbital region of the frontal lobes to the hypothalamic centres.

Dax and Radley-Smith (1946), in discussing the position of the cut, state that depression is best relieved by a lower incision, the aggression of the catatonic by a high one, and the paranoid schizophrenic may derive most benefit from the middle section combined with a horizontal one. With the lower incision there is more headache, drowsiness, restlessness, disinclination to eat, transitory neurological signs and usually a more rapid pulse rate.

Scarff and Kalinowsky (1947) turn back a small bone flap on both sides over the frontal lobes close to the midline and make incisions into the white matter in the coronal plane. There is less risk than in the "blind" operation. The results appear to be the same.

Pelaz (1947) injected blood into the white matter of the frontal lobe, so giving rise to a temporary leucotomy. If the results are good he suggests a permanent leucotomy. Woringer (1948*a, b*) injects a radiovisible and corrosive substance (uroselectan) into the brain through a trephine opening. His results are good.

Yahn *et al.* (1948) performed leucotomy in 3 stages, first one lower quadrant, then the other, and finally both upper quadrants in one operation. The interval between each operation varied from 1 to 6 months. In a group of 70 cases the results in the schizophrenics were better than with the standard leucotomy.

Yahn *et al.* (1948) carried out a parietal leucotomy, cutting the superior longitudinal fasciculus immediately above the ventricular junction. Out of 22 patients operated on, only 2—who had already undergone prefrontal leucotomy without improvement—showed improvement. The authors think that possibly where prefrontal leucotomy has failed there is a future for parietal leucotomy.

Poppen (1945 and 1948) has used the method of Lysterly with some small modification. He uses 2 trephine openings of 2.5 cm., removing a button of bone, 3.5 cm. from the midline immediately anterior to the coronal suture. A small dural flap is made. A ventricular needle is inserted into the most anterior part of the ventricle, then withdrawn and inserted in front of the anterior pole until the ridge of the sphenoid wing is felt. A lighted retractor permits the surgeon to see his way as he uses his electro-surgical suction unit. The white matter should be completely divided.

Meyer and McLardy (1948) found, in 40 cases examined post-mortem, that 22 had in both hemispheres what are described as "posterior" cuts, i.e. cuts involving the posterior half of the orbital region, the striatum, the pre-

motor region (areas 6 and 44 of Brodmann), the region of the external capsule, or any combination of these. All cases displaying general restlessness, vasomotor or trophic lesions and all displaying any of the miscellaneous sequelae, except epilepsy, were posterior cut cases. Damage to area 24 has apparently no causal connection with at least the rather gross types of clinical disorder.

Freeman (1949b), in a study of 100 cases of transorbital leucotomy, reviewed 1-3 years after operation, states that it is effective in chronic disturbed schizophrenics and in depressives who are relapsing after shock therapy, but are not considered disordered enough for a major leucotomy. Elder *et al.* (1948) used the transorbital approach in 11 cases out of 101, but were rather disappointed in the results and had decided to perform the radical operation. Fleming and Phillips (1949) have employed the transorbital method of approach with considerable success. They agree with Freeman that there is not the same personality disturbance as with the more extensive leucotomy. The incidence of post-operative epilepsy is very low.

TOPECTOMY.

Mettler (1944) found that bilateral removal of area 9 in a giant rhesus monkey produced both overactivity and over-reactivity.

Heath and Pool (1948) describe part of the work of the Columbia-Greystone Associates. A group of 24 chronic patients, together with 23 private patients, had various areas of the frontal cortex removed bilaterally. Of the 24 chronics, 11 were out of hospital 8 months afterwards. These 11 had areas 9 and/or 10 removed. Those who had more cortex than this removed developed tactlessness, irresponsibility and lack of remorse that so often follows leucotomy. These symptoms did not appear with removals confined to either areas 9 and/or 10. Of the 15 private patients, some of whom had been hospitalized for 28 years, and who had been followed for more than 3 months, 10 are able to function at their old capacity. The best area to remove appears to be the posterior part of area 10 and the anterior part of area 9.

There were no deaths; no patient with removal of area 9-10 has had a convulsion yet. Two cases in the private series in which posterior area 9 was removed had an occasional seizure during the first 4 post-operative days. Removals implicating areas 6 and 11 were more inclined to have seizures. One female psychopath has yielded a most encouraging result. The effect of the removal of 9 and 10 seems to be a damping down of emotion, but by no means its removal. Psychological tests showed that removal of 9 and 10 resulted in little or no loss in the ability for abstract thinking. Rorschach and Levy movement cards showed the altered affective response.

Le Beau *et al.* (1948a, b, c, d) at first removed areas 9, 10 and 46, but subsequently confined their excision to areas 9 and 10. They point out that the important region appears to be the junction of areas 9 and 10. There were no intellectual defects following operation. In 5 children operated on for psychomotor agitation and antisocial impulsiveness, the results were very good in two cases, good in one and partial in the other two. In those who were epileptic the result was not only mitigation of the psychomotor agitation, but also considerable decrease in the number of attacks.

Pool *et al.* (1949a) feel that in malignant types of schizophrenia which are deteriorating, topectomy should be performed without any unusually prolonged course of insulin. Feld (1949) found, amongst 27 patients operated on by bilateral topectomy, 15 good results and 8 medium ones. The best results were obtained in agitated oligophrenics, some forms of epilepsy and schizophrenia. By topectomy the intercortical communications are cut as well as the projecting fibres.

Le Beau (1949) found no personality or intellectual impairment after topectomy of areas 9 and 10. Topectomy of areas 9 and 10 in 10 cases of intractable pain was found superior to bilateral leucotomy because of lack of change.

Hardman (1949) does not feel satisfied with excision of areas 9 and 10. He had carried out a topectomy of area 13 on 3 catatonics, with a good result in one case. He had also carried out a bilateral excision of the gyrus cinguli and lips of the adjoining sulcus, i.e. a partial removal of areas 24 and 32. In the 12 cases the patient had shown improvement.

Spiegel *et al.* (1948) used a stereotaxic apparatus to produce lesions in the dorso-medial nucleus of the thalamus. This resulted in relief of nervous tension, anxiety and irritability without some of the side-effects of leucotomy. In patients with intractable pain, lesions were made in the mesencephalon and in the dorso-medial nucleus of the thalamus. Bilateral lesions in the vicinity of the commissura media diminished the frequency and severity of *petit mal*.

Wycis and Spiegel (1949), using a modification of the stereotaxic apparatus of Horsley and Clarke, which they called a stereo-encephalotome, performed either a thalamotomy (a lesion in the dorso-medial nucleus), or a mesencephalotomy (a lesion in the spinothalamic tract in the mid-brain). The lesions are produced by electrolysis.

Scoville (1949), from a study of 124 cases of selective cortical undercutting came to the following conclusions: (1) Orbital undercutting is the ideal operation for severe psychoneuroses, because of its technical facility and almost complete absence of personality blunting. (2) Undercutting of the superior convexity works well for certain types of pain and addiction. (3) Orbital and superior convexity undercutting benefits the affective and schizophrenic psychoses. (4) Cingulate gyrus undercutting should be used for research. (5) Standard lobotomy to be reserved for the "hopeless" deteriorated schizophrenic of many years' duration. McKissock (1949) has also, in this country, carried out the operation of undercutting, using his own method, literally sucking out the white matter from under areas 9 and 10.

COMPLICATIONS.

Petersen and Buchstein (1942), in a series of 46 cases, found flushing and sweating in most cases, and a lowering of blood pressure and a slowing of pulse in each case. In 4 out of 5 cases studied there was a decided increase in free hydrochloric acid.

Kisker (1944) points out that destruction of prefrontal tissue does lead to the release of widespread autonomic symptoms in the form of vasomotor

disturbances, flushing, sweating, lack of sphincter control, restlessness, etc.

Hemphill *et al.* (1942) found an increase in the output of 17-ketosteroids following leucotomy, probably due to hyperactivity of the adrenal cortex due to increased production of cortico-trophic hormone, this in its turn being due to interference in the pathway between the frontal lobe and the hypothalamus. Kisker (1944) considers drowsiness the most generally observed post-operative neurological sign. This has not been our experience.

Reitman (1945) describes the effects of drugs which influence the autonomic nervous system, i.e. prostigmine, eserine, ephedrine and benzedrine. He considered that after leucotomy there was an increased resistance towards drugs which upset autonomic equilibrium. Ziegler and Osgood (1945) found that, of 17 patients submitted to leucotomy, 6 had bilateral oedema of the feet and legs, and in 4 of these it was associated with tenderness. Of 8 patients (from this group of 17) with complications referable to the legs, 6 had occasional incontinence of the bladder and rectum for considerably more than a month. Kindwall and Cleveland (1945), in a series of 15 cases of hopeless prognosis, most of which had received shock treatment, found oedema, blister formation and sometimes tenderness and pain in one or both legs during the first month in a number of their cases. This is probably a trophic disturbance due to some effect of the section on areas 6, 8 or 32.

Reitman (1946b) studied the effect of leucotomy on gastric function. The section was assumed to sever fibres coming from areas 11 and 12. He found that the volume of gastric juice produced under the influence of prostigmine was considerably increased, but there was no increase in production of HCl.

Reitman (1946a) found, after leucotomy, a slight increase in total gastric acidity, the peak of acidity is reached earlier and the emptying of the stomach takes place more rapidly. When 1 mgm. of prostigmine is injected intravenously there is a relative increase in the total volume of the gastric juice.

Sargent (1946) reports a case of intractable dermatitis which was cured by leucotomy, but returned when anxiety returned 2 years after.

Frank (1946), in 200 cases, found urinary incontinence in 15 per cent., but all recovered from it in 6 months. Nine per cent. had major epileptic fits, but all responded to anti-convulsive medication. Eighty per cent. of these had had a posterior cut. Some of the early cases showed a peculiar sagging in posture, but this disappeared. One case developed choreiform jerking of the limbs and involuntary grimacing. Seven female cases developed hirsutism.

Wohlfahrt (1947) found incontinence persisting in only 4 per cent., and seizures in 4 per cent. One patient showed transitory contractions in the knee-joints. Broager (1947) encountered in two patients urticaria-like skin affections with oedema and redness of the skin at all points of pressure, even where the bedclothes touched the patient. One of these patients died from the cut being too far back, possibly causing a lesion in the anterior part of the thalamus.

Wiesel and Izikowitz (1947) found incontinence of urine in most of their 60 cases. In 10 cases they found contractures of the flexor muscles of the knee-joints develop 2-4 weeks after operation. Some cases developed oedema of

the ankles. These contractures eventually disappeared completely in all but 2 cases. Three cases developed hemiparesis and another a mask-like face; this symptom disappeared after 6 weeks. Two developed fits, one after 9 days, but no more for 10 months at least, the other, one fit after 15 months and another at 20 months.

Wohlfahrt (1947) found, in cases operated on under local anaesthesia, an immediate shock effect of the sympathetic paralysis type. With his blood-sugar tests he found that almost immediately after the operation the patient's sensitiveness to adrenalin was increased. Afterwards there was a stabilization of the vegetative system, but on a lower level, which corresponds with the relief of emotional tension shown clinically.

Rinkel *et al.* (1947a), from investigations on 29 leucotomies and a group of controls, consider that there is cortical representation of the autonomic nervous system in the prefrontal area. The rise in blood pressure after epinephrine was twice as great in patients after leucotomy as in the controls. The carotid sinus slowing of the heart was pronounced in 84 per cent. after leucotomy. Following the slowing of the heart, the E.E.G. in 92 per cent. of cases presented high-voltage slow waves of the 5-9-per-second frequency range. Loss of consciousness and tonic-clonic convulsions occurred in 88 per cent. following the appearance of these slow E.E.G. waves. The authors found that benzedrine sulphate and atropine, if given in sufficient amounts, seemed to abolish the carotid sinus reflex, whilst acetyl-methyl-choline enhanced it.

Rinkel *et al.* (1947b) found that positive carotid sinus reactions were present in almost all patients after leucotomy, and conclude that the operation liberates the parasympathetic or cholinergic system from a certain degree of cortical inhibitory influences. The over-reaction of the adrenergic system to epinephrine indicates that this system, too, is subject to cortical control from the prefrontal area.

Kennard *et al.* (1947) found in cats in which sham rage had been produced by bilateral frontal lobectomy that the blood-sugar level is increased, and may continue raised for some 4-5 hours, with an accompanying rise of pulse and respiratory rate. There was no rise in blood pressure. In monkeys which do *not* develop sham rage after cortical ablations there is no significant change in blood sugar, pulse, respiration or blood pressure.

de Greeff (1947) found increased responsiveness to E.C.T. after leucotomy.

Reed (1948) gave an Ewald test meal to 9 persons before and after leucotomy. All showed either anacidity or subacidity before, and either normal acidity or hyperacidity afterwards.

Puech (1949) found, in 72 per cent. of lobotomies, organic changes present, i.e. thickening of the leptomeninges, serous meningitis, venous stasis, cerebral atrophy, etc.

PSYCHOLOGICAL CHANGES.

Strecker *et al.* (1942) found a disappearance of dangerous and destructive tendencies in a small group of schizophrenics. Two showed a striking revival of pre-psychotic artistic accomplishment.

Harlow and Spaet (1943) found that the scores of 2 monkeys who had had their prefrontal association areas removed were consistently inferior to those of the controls.

Allen (1943) found in dogs conditioned to respond to pairs of stimuli in three modalities who had had leucotomies performed on them, that in general there were no permanent effects on the conditioned responses or the conditioning process.

Kisker (1943*a*) points out that after leucotomy there is a re-distribution of emphasis in the emotional sphere, what he calls an attitude modification which corresponds to Freeman and Watts' alteration in the consciousness of self and a disturbance of the orientative mechanisms. There is also a reorganization of the dynamic equilibrium of the organic substrate, which shows itself the moment the second side section is completed by a relaxation in worry, anxiety and apprehension. Fleming made the observation that in 2 patients operated on in 1941, under a local anaesthetic, both said they thought they had died at that moment, and were surprised to find that they were still alive!

Kisker (1943*b*) found no pattern characteristic of post-leucotomy patients. To a certain extent there was evidence of the occurrence of organic signs suggestive of intracranial damage. He (1944*a*) thinks that clinical improvement may appear in the absence of improvement in abstract behaviour, and there may also be decided improvement in abstract behaviour without any clinical improvement. He (1944*b*) considers that the presence or absence of post-operative depression or euphoria is more a function of the pre-operative personality than it is of the plane of section. He does not consider that confusion occurs after the operation; what he would describe as disturbance of the time-schema, space-schema or body-schema does. He does not agree with Freeman and Watts' statement that undue mental alertness in the immediate post-operative phase is a sign prefacing relapse. He (1944*c*) found 6 signs, on Rorschach examination, which appear to dominate the post-leucotomy pictures; these include low F +, low R, lengthened reaction time, lack of M.C and Z responses, and a relatively high proportion of H and Hd responses. As, however, these signs rather tend to occur in pre-operative records as well, it is felt that they are more a function of the psychotic process than of the leucotomy.

Lashley (1944) has shown that maze performances in the rat were not impaired by long incisions through the cortex and underlying fibres. If deterioration of performance did occur it was due to interruption of the thalamo-cortical fibres or to the destruction of cortical tissue. There was no deterioration as a result of transcortical interruption.

Watts and Freeman (1944) found in 45 cases of obsessive tension states that there was no significant intellectual or emotional impairment. Those patients who were previously handicapped by obsessive tension states showed an improvement in pragmatic intelligence after leucotomy. As Jaeger (1944) points out, "These people may not be more intelligent after operation, but they can use what they have better than they could before."

Porteus and Kepner (1944) state that they found in a series of 20 cases that there was no consistent picture of general mental impairment arising

from leucotomy. They found, however, an average loss of 3 points in I.Q. and the Maze test, demonstrating very clearly a loss of planning capacity and initiative; there was an average loss of 2 years. In successive trials of the Maze there was a strong tendency to repeat identical errors: 29.36 per cent. compared with 6.73 per cent. in normals, 8.10 per cent. in delinquents and 12.25 per cent. in feeble-minded patients. This repetition of errors, which appears to be characteristic of post-leucotomy patients, is due to a lack of initiative, an unwillingness to try new approaches to a problem.

Watts and Freeman (1945) consider that there is no impairment of intelligence after leucotomy in obsessive tension states.

Campbell and Harlow (1945), in a group of 6 rhesus monkeys that had had bilateral prefrontal lobectomy performed, found that they showed defect in attention and increased distractibility. There was impaired performance on many different kinds of test.

Schrader and Robinson (1945) used the Gardner behaviour chart in assessing the result of leucotomy in schizophrenics. They found an improvement from a pre-operative mean of 1.25 to a post-operative one of 2.53. The greatest improvements were in attention to personal behaviour, sociability, willingness to follow directions, and work initiative when supervised. There was least improvement in sleep, care of property, work capacity and work initiative when alone. A pre-operative Gardner index of less than 0.75 suggests marked deterioration, and may be regarded as a contra-indication to leucotomy.

Yacorzynski and Davis (1945) found, after lesions of the frontal poles, that (1) a longer time and more illumination were required to perceive geometrical figures and words, and that (2) the subjects were unable to perceive as many meaningful objects in ambiguous figures as the controls, that (3) the illusory effect of the Müller-Lyer illusion was exaggerated and the illusory effects of many other visual illusions were not perceived, (4) the patients were unable to recall as many objects exposed visually as the controls, and (5) were unable to perceive reversals on many of the figures with reversible perspectives, and if reversals occurred, their frequency was below average.

These differences, the authors think, may mean that (1) a longer time is required to perceive a stimulus, (2) the number of situations which are perceived in a stimulus field is decreased, (3) there is an inability to shift readily from one stimulus to another, and (4) there is a distortion of normal perceptions.

Halstead *et al.* (1946) found, in a small group of 8 patients, that there was no evidence of a shift in the impairment index compared with the condition before operation.

Frank (1946) found, in his series of 200 chronics, no intellectual impairment 12 months after operation, except for the over 55 age group, who showed a discrepancy of their vocabulary, verbal and performance scores. A number show an over-politeness which disappears after a year or so. Brody (1946a) found no difference in the results of intelligence tests before and after leucotomy. Goldstein reported that an analysis of the patients' behaviour showed evidence of deterioration, yet the Goldstein tests failed to show deterioration in abstract thinking.

Robinson (1946) studied 10 leucotomized patients in detail. She found

that all showed a lack of deliberateness or prolonged attention. They did significantly less well than the controls on two tests demanding deliberation (rhymes and numbers), they also did less well on tests demanding deliberative behaviour (Downey's Speed of Decision, Volitional Preservation and Motor Inhibition).

Brody (1946*b*), as a result of investigation with a variety of intelligence tests, was satisfied that as a result of leucotomy there was no impairment of intelligence. He points out that ideas formerly held with great emotion may remain unchanged after operation but stripped of the emotion, and that this fading of the emotion may precede fading of the ideas.

Golla (1946) considers that the post-leucotomy personality exhibits a purely objective mentality. Fear, anger and affectivity are manifested within normal limits, but the subject does show an impairment of the power of ethical valuation. As time passes, the post-leucotomy patient shows a return of the power of self-objectivation, the sense of personal responsibility. The central nervous system must never be regarded as a rigid inflexible machine, but must be seen as a flexible organic whole which, if it cannot arrive at its goal by one route, will arrive by another, though possibly more circuitous one.

Goldman *et al.* (1946) point out that in brain damage, information and comprehension are least affected; these, together with vocabulary score, educational level and occupational attainment, give the best estimate of original endowment. The ability to reverse digits implies some flexibility in mental function. The ability to perform complicated calculation may or may not be impaired. Digits and arithmetic are tests of attention and concentration. The similarities test shows up brain damage most clearly; hence the Shipley-Hartford scale shows up brain damage very well. Non-verbal tests yield the most significant data concerning brain damage on picture-completion test. Slowness of response, inability to find a name for one object, acceptance of incomplete as complete, and reaction to insignificant details or description of the pictures are all typical. There is a lack of ability to understand a picture as a whole. Block-design is usually badly done and without insight. The tendency to repeat errors on a given design is an example of rigidity.

Reitman (1947), after analysis of the artistic products of two leucotomized schizophrenics, considered that their personalities were stimulated and artistic reactions developed. The artistic productions showed a rapid development towards organized form-tendencies, normal symbols and patterns.

Glees (1947) found that monkeys previously fierce became tame and docile, while others became restless. Maurice and Trotot (1947) describe a case with a tumour involving the central grey matter which showed a marked tendency towards joviality.

Rylander (1947) carried out psychological investigations on a small group of cases within 12 months of operation. He measured the intelligence by Binet-Terman and Terman-Merrill, L. and M., and used a battery of tests. The patients themselves indicated that their emotions had lost richness and depth, and interests had diminished. The relatives reported that they had lost initiative and were indifferent and careless. There was also a deterioration in the ability to do intricate manual work. From the results of his test

examinations he found no impairment of memory. There was a slight lowering of intelligence, and a decrease in the ability to handle abstract concepts. The noun enumeration test showed a distinct falling off. Although the time of observation was under one year, the author thinks the likelihood of improvement is not great.

Ödegård (1947) puts forward the interesting suggestion that the intellectual capacity of the leucotomized patient is not reduced, because man does not use all his cortical cells, possibly only uses a fraction of them and, therefore, has a considerable reserve to fall back on when required. Animals are divided according to their degree of cephalization into various levels, the lowest level being that of the shrew-mouse; next, on level 2, come mice, porcupines; on level 4 hares and the more primitive carnivora; on level 8, dogs, cats and most ruminants; on level 16, bears and anthropoid apes; on level 32 the Malay bear and the Capuchin monkey only; and on level 64 man by himself.

Stevens (1948) states that the post-operative personality is significantly altered, displaying high distractability and a tendency to simplify the reaction to the environment.

Friedlander and Banay (1948) give a detailed account of one patient suffering from a sexual psychopathy. Seen some considerable time after the leucotomy, he was obviously deteriorated by clinical standards. He had an Army Alpha Test age of 16 $\frac{5}{12}$, a Wechsler I.Q. of 105, on Kohs' Block functioned at 9 $\frac{7}{12}$, and Knox Cube Test at 7 years. With the Porteus Maze Test he acted like the feeble-minded group in showing no practice effect. Robinson's Deliberation Test, designed to separate lobotomized from non-lobotomized patients, placed him in the lobotomized group. The Vigotsky Blocks Test and the Babcock-Levy Test both showed significant changes. Beck himself administered a Rorschach test and reported: "The reaction pattern appears to be characteristic for patients with a pathologic process of the brain which has not gone far, since a residue of higher functioning persists."

Garmany (1948) considers that restitution of the pre-morbid personality after leucotomy may be expected as a rule. He thinks that no permanent personality change occurs which is attributable to the leucotomy alone. Rehabilitation is usually necessary, especially if the home surroundings are not too good.

Hutton (1948), in studying a patient 9 weeks after leucotomy, suggests that creative imagination was much reduced and almost non-existent. She found that emotional motives and associated judgments of value are not apparent, and that there was some decrease in effort and application.

Elonen and Korner (1948) found, in a case of left frontal lobectomy in a man of 52 an improvement of I.Q. from 62 to 111 on the Stanford-Binet, and on the Kuhlman a rise from 53-80. On the other hand, his Rorschach responses showed interference with general functioning as found in patients with severe organic pathology, but an increase in productivity, the ability to project, and versatility.

Settlage *et al.* (1948), comparing 5 normal monkeys with 5 leucotomy monkeys, found that the performance of the latter was distinctly below the former. The best score of each operated animal was worse than the

worst score of each normal animal. The authors consider that the poor performance was largely due to perseverative interference, i.e. from impairment of the ability to relinquish previously-acquired, interfering reaction patterns.

Stengel and Carse (1948) could not confirm that there was any change in the attitude towards religion in a series of 320 cases of leucotomy. They consider that the indications for leucotomy are chronic schizophrenia and depression, and involutional depression with agitation and dysphoria.

Haddenbrock (1949) considers that the personality changes which follow leucotomy, or what he calls "defrontalization," consist of a demolition of the self-aware ego, decreased associative power with affective blunting. The disease, whatever it may be, is not changed, but the patient's attitude towards it is.

Furtado *et al.* (1949) consider that although the intellectual changes are small, the personality changes are serious because of the affective indifference caused. On these grounds they consider leucotomy as quite a last resort in treatment.

POST-OPERATIVE CARE AND REHABILITATION.

Ewald and Freeman (1947) discuss the nursing problems of leucotomy. They point out that many patients behave childishly, and have to be treated and trained like emotional children. It is rather shattering to read that "sometimes punishment (preferably spanking) may be necessary; the patient reacts like a child and harbours no grudge." The authors prefer home to institutional nursing.

Farmer (1948) emphasizes the importance of post-operative rehabilitation. He says it must be immediate and must be "pushed." All post-lobotomy patients require a specialized programme of vocational, avocational, social, recreational and physical education. This scheme can only be carried out in a controlled hospital environment, and shows the folly of too early discharge after operation.

Solomon (1949) draws attention to domestic difficulties as a bar to recovery. He points out that when the patient returns home, the relatives need careful advice, continuing guidance and encouragement.

This we have found to be a very important factor in recovery, and we have come across a number of cases where domestic and financial difficulties have proved a great hindrance to recovery. There are factors which have been active for years, and which it has been impossible to cope with, i.e. one case where a man had "done" his son-in-law out of £5,000, which he had promised him when he died, and then altered his will. "Difficult" wives and husbands can make a great difference to a patient's recovery, especially those who are "getting their own back" after years of endurance of the patient's pre-operative symptoms. A very good account of a rehabilitation programme is given by Burlingame (1949).

SEIZURES.

Parker (1946) states in his series of 100 female patients that seizures were fairly common in the first 24 hours. Ström-Olsen (1946) found that out of

95 non-epileptic cases, 6 developed seizures. Frank (1946) found 9 per cent. of epileptic seizures, mostly after the elapse of 6 months. No cases had fits after 8 months from operation. Mosovich and Stevens (1947) report 33 per cent. of seizures in a series of 24 cases.

Watts and Freeman (1948), in 531 cases, found a seizure incidence of 12.3 per cent., the seizures generally occurring about a year after operation. After a second lobotomy the incidence is much higher—47 per cent. Fifty per cent. of the patients developing seizures had been given E.C.T. before operation, but no account is given of how many of those who did not have seizures had had E.C.T. prior to their operation.

RESULTS.

Govindaswamy *et al.* (1944) operated on 25 Indians, mostly chronic schizophrenics of 3-7 years' duration. Seven recovered, 6 improved and 2 became worse.

Berliner, F., *et al.* (1945) report on 100 cases. Four died and, of the remaining 96, 29 recovered, 16 are much improved and 14 improved. No patient was made worse.

Matulay and Zucha (1946) operated on 48 long-standing schizophrenics, and found that of 36 who survived the war, 12 were discharged from hospital, of whom 7 were living satisfactorily at home and 13 could be regarded as improved. Moore (1946), in 150 cases, found excellent results in obsessional states, encouraging results in chronic melancholia and a remarkable change in outlook in schizophrenia. Parker (1946), in a series of 100 chronic female patients, found of 39 melancholics that 30 recovered, and of 33 schizophrenics, 10 recovered but 3 relapsed. Of the 10 recoveries, 3 were catatonic, 3 paranoid and 4 hebephrenic. Of 19 cases of paranoia and paraphrenia, 5 recovered, of whom 2 relapsed. Frank (1946) reports results on 200 chronic cases of average duration $4\frac{1}{2}$ years. All had proved refractory to various forms of treatment. The age varied from 22-69. Of the paranoid schizophrenics, 25 per cent. showed a social recovery. Hebephrenics with a "giggly" affect and simplex cases with marked emotional blunting were very disappointing—in fact, might be included amongst the contra-indications. The schizophrenic patient should be kept in hospital post-operatively as long as possible. Their rehabilitation should be very gradual. Of the total 200 cases, 42 per cent. showed a social recovery and a further 28.5 per cent improved. Falcon (1946), amongst 45 cases of leucotomy, found 50 per cent of cures, 20 per cent. improved.

Moore (1946), in a series of 150 of very bad prognosis, found 56 discharged to their homes. He considers that improvement can continue for as long as 3 years. He goes so far as to say that leucotomy should not be carried out unless facilities exist for expert rehabilitation.

Ström-Olsen (1946) presents a table of undesirable mental symptoms which were observed after the patients had gone home. The principal symptoms, in order of frequency, were selfishness, egocentricity or inconsiderate behaviour; deterioration of personal habits or manners; aggressiveness; irritability; lessening of affection and apathy. Yahn (1947), in Brazil, operated on 209 cases, 161 by the original Moniz' technique and 48 by Freeman

and Watts' method. In 180 schizophrenics, 24 recovered, 6 improved and 3 died. Sargant and Stewart (1947) describe a good result in a neurotic reaction of hysterical type produced by battle stress and little improved by prolonged psychotherapy, insulin or large doses of barbiturates. There was a good family history as well as a good pre-morbid personality.

Solomon (1947), in a group of 23 hopeless schizophrenics of long standing, found 11 of them fit to go home and 5 much improved. He was struck by the warmth of feeling shown by them, expressing affection for their families, and by the fact that instead of being less moral after operation they were more moral. Knobloch (1947) reports 103 cases, 26 cases operated on by Moniz' method, considerable improvement 3 cases, some improvement 12, no deaths; Duff's modification, 25 cases, considerable improvement 5, partial 11, and 1 death.

Myerson and Myerson (1947) found good results in 4 women over 60. Three out of the 4 made excellent social readjustments. None was affected intellectually. Tension and depression were relieved.

Mosovich and Stevens (1947) report 24 cases. They found two main types of post-operative personalities, the slow and restrained one, and the hyperactive. The most common feature in the personality after operation was a tendency to simplify all reactions. Although the cases were all of bad prognosis, most were improved.

Frankl and Mayer-Gross (1947) consider, from the results in 68 cases, that the prominent features are well-known symptoms of frontal lobe damage due to trauma or neoplasm. Blomquist (1947) reports results on 32 schizophrenics of long standing, of 8 year's average duration. Three were discharged and sent home, 12 were considerably improved, 2 died from intracranial haemorrhage, and 2 from other causes. Ellerman (1947) reports 14 cases in severe and long-standing schizophrenics of hopeless prognosis. Two were regarded as much improved, 4 as improved, and 1 as much worse. Ellebjerg (1947) reports results on 84 cases, 18 much improved, 21 improved, 39 unchanged, 1 worse and 5 died. Wohlfahrt (1947) operated on 48 patients, and found 20 greatly improved, and 9 improved, 2 died. One case of torticollis with depression recovered from both conditions! Among his schizophrenics the paranoid cases provided the best results, the hebephrenics the worst. Depression, hallucinosis or delusions accompanied by anxiety, in some cases also catatonic symptoms were regarded as indications for operation.

Wiesel and Izikowitz (1947) report results on 60 cases of hopeless prognosis and duration of from 1-20 years, only 2 with duration less than 2 years. Eleven showed considerable improvement, 8 moderate, and 11 slight improvement. In some of the cases the result is described as nothing short of miraculous. Those which were not recovered or improved were changed from depressed and anxious to irritable and aggressive.

Stevens (1948), from a study of a small series of 30 chronic patients, of which 9 were schizophrenics, found 7 improved and one a social recovery. One tuberculous schizophrenic made a splendid recovery.

Vencovsky and David (1948), in cases of schizophrenia, found their best results with cases of catatonic and catatonic-hebephrenics. The simple and

hebephrenic groups gave least response. In the manic-depressive group the best results were with simple melancholias, or with those of periodic course followed by involutional melancholia. After the operation nearly all patients showed striking changes in personality. Ricard and Girard (1948) consider that conflict between the two hemispheres is responsible for many neuro-psychiatric affections. On this hypothesis he performed 3 left unilateral prefrontal leucotomies, with 2 lasting and 1 transient improvement. Ibor (1948) found that among 40 chronic schizophrenics the majority were able to go home after leucotomy.

Eringa (1948*b*) describes 50 per cent. recoveries in a series of 16 chronic schizophrenics. Coheen (1948) found that patients made a partial adjustment during the few months after leucotomy, but appeared to reach a "plateau" of improvement that lasted, on the average, for 1.5 years. After that time they showed continued improvement. There was a replacement of the disturbed emotional pattern by ranging degrees of sluggishness.

Hoffman (1949), in a group of 42 schizophrenics of from 2-20 years' duration, obtained good results; 30 became neat in appearance, ate and slept well, partook of group activities, were polite and orientated. None of the 42 was completely self-supporting. The writer considers that an organic brain defect has been substituted for the psychosis.

Worthing *et al.* (1949) found, in a series of 350 cases, that 43 per cent. of cases of less than 3 years' duration left hospital, 20 per cent. of those from 4-7 years and 6 per cent. of those over 7 years' duration. In those who did not go home, there was a clear-cut improvement in behaviour which was slow but permanent. The writers found very little post-operative personality change of malignant type.

Frank (1946) found 4 relapsed out of 84. Hutton (1947), in 3 cases made worse by leucotomy, points out that before operation they showed egoism, lack of social adjustment, poor work record, lack of achievement and little evidence of altruistic affection. Torras and Fuster (1949) performed leucotomies on 21 cases of terminal dementias in schizophrenics, with disappointing results.

DEATHS.

Ström-Olsen (1946) in 116 cases had 4 deaths, all due to cerebral haemorrhage. Frank (1946*a*) had 2.5 per cent. deaths, 4 of cerebral haemorrhage and 1 staphylococcal meningitis. Three died of intercurrent illness more than a year after operation. Parker (1946) had 2 deaths from cerebral haemorrhage in his 100 cases. Frank (1946*b*) lost 5 out of his 200, 4 from cerebral haemorrhage. Three died from intercurrent illness more than a year after operation. Wohlfahrt (1947) had 4 per cent. deaths amongst 48. Broager (1947) leucotomized 90 patients and had 5 deaths, 2 from haemorrhage into the opened lateral ventricle, and 3 because the lower part of the incision was too far back. Wiesel and Izikowitz (1947) had 7 deaths out of 60 cases. Two cases died without direct relationship between the operation and death. Two died from infection of the operation area, 3 from intraventricular haemorrhage.

Eringa (1948*a*) found in one case that died in 48 hours from cerebral

haemorrhage that the cut was too far posterior so that the lateral ventricle had been opened. The third ventricle did not contain blood, but the fourth was completely filled up by a blood-clot, and this had obviously been the cause of the death.

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SUICIDE.

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THE phenomenon of suicide has cultural, philosophical, religious, sociological, psychopathological and clinical aspects. This review is concerned with some of these aspects only. The idea of self-imposed death has always had a peculiar fascination for mankind. There are strong indications that, apart from a decline during war, the suicide rate has been on the increase for some time. Considering the fact that medical men, and in particular psychiatrists, are constantly concerned with this problem, it is indeed surprising how small their contribution to its elucidation has been. K. Menninger (1938, 1947) suggested that a strong unconscious resistance, similar to that which made medical men shun the study of sexual behaviour, was responsible for their failure to give suicide the attention it deserved as an individual and mass phenomenon. The clinical psychiatrist is, as a rule, ill-equipped for the study of suicide unless he is willing to include the sociological and general psychopathological aspects into the orbit of his interests. Only a proportion of suicides can be understood as the outcome of mental illness in the clinical sense. The study of suicide, which has rightly been described as our most baffling social disease, is a task for social as well as clinical psychiatry and psychopathology.

Several contributions have in recent years, as in the past, come from psychiatrists who concerned themselves with the incidence and the prevention of suicide among the patients under their care. Others have studied the occurrence of suicide in the general population of certain areas or countries. Useful information has been supplied by statisticians who, for various purposes, are following the fluctuations of the suicide rates. Suicide has medico-legal implications, some of which have been the subject of recent publications.

A considerable number of writers have studied the urge for self-destruction, its origin and its effects on human behaviour. Freud's theory of the death instinct and of its fusion with libidinal tendencies has stimulated research into the psychodynamics of suicide. In these researches suicide has been studied against the wider background of ubiquitous destructive tendencies. While some writers set out to trace the various ways in which the self-destructive tendencies may colour and modify human behaviour and personality, others have tried to demonstrate the important part that the life instinct, i.e. the libido in its various forms, plays, even in the act of suicide itself.

Thus psychopathology is attempting to study the sources of man's attitudes to life and death, to which hitherto only religion and philosophy have given expression and interpretation.

General Surveys : Incidence : Clinical Psychiatric Studies.

Henderson (1938), reviewing the problem of suicide from the point of view of social and clinical psychiatry, divides suicidal cases into three groups : (1) cases in which the diagnosis is open to argument and in which the exogenous factors appear more or less adequate, but operative only in specially predisposed persons ; (2) cases of neurosis, psychopathic personality, sexual inversion and schizoid states in which the attempted suicide may appear motiveless, yet dependent probably on deep emotional conflicts ; (3) cases of mental disorder in which there is a constellation of etiological factors, endogenous and exogenous. If there were any sane suicides they should be found in the first group. However, the author states that, in his experience, he has never found one who might be considered of sound mind at the time the act was committed, even if it had been planned with great forethought and premeditation. Henderson admits the importance of the psychoanalytic contribution to the understanding of the psychodynamics of suicide, but regards its study and prevention chiefly as a problem for social psychiatry. Deshaies (1949) expresses similar views, and lays particular stress on the part that religion and education have to play in the prevention of suicide by teaching moral principles and fostering the sense of solidarity with the community.

Gruhle's (1940) monograph on suicide was not available to the present reviewer. The summary reprinted elsewhere suggests that the book is a compilation of previous studies by the same author. He states those factors which contribute to an increase and those which make for a decrease of the suicide rate. To the first group of factors belong economic crisis, high density of population, employment in industry, residence in large towns, certain professions such as domestic service, Protestant religious affiliation, increasing age, widowhood, divorced state, childlessness, alcoholism, psychopathic personality, psychosis. The proportion of psychotics among suicides is small. The significance of the racial element is still obscure. Among factors leading to a reduction of the suicide rate he found : permanent emotional ties, favourable economic circumstances, low density of population, rural occupation, Roman Catholic religious affiliation, youth, the married status and a large number of children. The following two articles dealing with special aspects of suicide appeared after the monograph.

In the first article (1940), Gruhle discussed the geography of suicide. He assumes that mental illness is responsible for not more than 10 to 20 per cent. of suicides. Possibly geographical variations in the incidence of suicide are related to differences in the incidence of psychoses. Greater density of the population is probably mainly responsible for such differences in the incidence of suicide as exist between Denmark, with 18, and Norway with only 5.8 suicides to every 100,000. Gruhle compares the pre-war rates in various parts of Germany. A higher standard of living, an over-aged population, frequency of divorce make for a high suicide rate. Roman Catholic districts have a lower suicide rate than districts with a mainly Protestant population. A high incidence of crimes of violence is correlated with a low suicide rate.

In another study (1941), Gruhle dealt with the incidence of suicide in old age. While the suicide rate in juveniles showed a steady decrease in pre-war

Germany there was a marked increase of suicides in persons over the age of 60, both in the rural and in the urban population. Psychosis of old age only rarely leads to suicide; 4,200 out of 20,000 Germans who took their lives every year were old people. Gruhle believes that the following motives play a part in suicide of old age: (1) Awareness of physical and mental decline. (2) Weariness of life, in such cases life is thrown away because it has become stale. (3) Refusal to adapt to changed circumstances; enforced idleness and loneliness are important factors. Aged spinsters are less prone to suicide than childless widows. The highest suicide rate was found among divorced men between 61 and 70. (4) Illness felt to be incurable. The decrease of the suicide rate in war is less marked among the aged than in the other age groups. The suicide rate among old people does not show seasonal fluctuations to the same degree as among younger age groups.

Ogburn and Nimkoff (1947), discussing suicide from the sociological point of view, blame the impersonality of city life for the frequency of suicide among large town popularions. They point out that it is easier to be lonely in a large city than in a small town where there is a closer identification with the group. It is worth mentioning that T. G. Masaryk (1881) made similar observations in his classical study on suicide as a social mass phenomenon of modern civilization.

The suicide rates for England and Wales, reported in *Criminal Statistics*, have shown a steady increase in recent years, after a marked decrease during the war, but they are still below the 1938 figures. The actual figures for successful suicides in 1948 were 2,900 males and 1,704 females, as compared with 2,740 and 1,587 respectively in 1946, and 3,531 and 1,732 in 1938.

The *Statistical Bulletin* of the Metropolitan Life Insurance Company (1942-1945) contains interesting information about the decline of the suicide level in America during the war years. In 1944 the suicide death rate among those insured, as in the general population of the U.S.A., established a new low record of 5.3 per 100,000, as compared with 13.3 in 1911, and 10 in 1933. Actually, the downward trend had begun about the time of the outbreak of war in Europe, being 8.5 in 1940. The general pattern of reduction was quite different for the two sexes. While in males the decline was most marked in the older age groups, where the toll from suicide is heaviest, in females the decline was much more marked in the younger age groups. The highest proportion of successful suicidal attempts was found in cases of ill health. Suicide tends to vary inversely with the curve of business conditions, but this does not apply invariably. In an investigation into the causes of suicide, carried out in Detroit in 1942-43, less than 2 per cent. were attributable to financial difficulties. The decline of the suicide rate during the war is attributed to more favourable economic conditions, as well as to certain psychological effects of war which increases the sense of usefulness and strengthens emotional ties. The decline is more marked in males than in females. The male-female ratio among policy holders was 3 in 1921-23, 3.6 in 1931-33, and 2.7 in 1941-43. Methods of suicide have shown only slight changes during the past 25 years. The four leading means of suicide in men have been shooting, hanging, gassing, and poisoning in order of frequency. In recent years hanging has become more

frequent among men. Poisoning, which in the past was the leading method in women, now ranks second.

Dahlgren (1945) made a statistical and psychiatric review of suicide and attempted suicide occurring in Malmö from 1933 to 1942. His group comprises 300 cases. The suicide rate remained, on the whole, stable during the period under survey, though in males it showed a slight decline from 1938. The importance of the various factors which are generally regarded as significant for the incidence of suicide, such as unhappy love, marital and economic troubles, are examined statistically. The psychiatric aspects of suicide are fully discussed. It is pointed out that even in depressive psychoses individual motivation may play a part. (The book was reviewed in *J. Ment. Sci.*, 93, Jan., 1947, p. 115.)

Palmer (1941) and Reitmann (1942), each studying the histories of 25 cases of attempted suicide, found that in the majority of their cases one or both parents had not been available as love objects in childhood. In Reitmann's view such a childhood history should be taken into account when the likelihood of suicide is considered in an individual case.

Boven (1942) finds the same factors correlated with high suicide rates in Switzerland as other writers elsewhere. Switzerland has a comparatively high suicide rate. Boven regards the suicide index as an indicator for the frequency of psychoses, especially of schizophrenia. He regards every schizophrenic, schizoid psychopath, manic-depressive, and cyclothymic as a potential suicide.

Shimshony (1941), also working in Switzerland, found a correlation between the consumption of alcohol of a population in a given area and male mortality in general, and mortality from suicide in particular.

Speijer (1948) studied the incidence of suicide among Jews in the past and in recent times. In ancient Jewish civilization suicide was neither forbidden nor approved of. The suicide rate among Jews has shown a steady increase since the latter half of last century, and has for some time been higher than among other groups. The author attributes the high incidence of suicide among Jews partly to environmental difficulties (the Jewish suicide rate always rises steeply in times of persecution), and partly to their predominantly cyclothymic predisposition.

McGeorge (1942), in a study of 523 potential suicides in Australia, noted that December was the peak month. The peak hours of the day were 10 a.m. and 10 p.m., the former for men, the latter for women; 70 per cent. of the cases belonged to the age periods from 20 to 50. The commonest cause in this group was an abnormal mental condition. Unemployment and financial difficulties played a relatively small part.

Arief, McCulloch and Rotman (1948) studied statistically 500 cases referred to them by the judges of an American Municipal Court. Fake attempts were frequent under the age of 30. In younger age groups females outnumbered males, but with increasing age the proportion of males increased. Alcoholism was a precipitating factor in almost half the cases over 20. Forty-one of the 100 cases studied in detail had an inadequate work record. All psychiatric categories were represented. A high proportion had suffered disappointment

in love. The majority required active psychiatric treatment. In many a sense of guilt and a desire for punishment was noticeable.

Prudhomme (1941) found a total of 67 deaths from suicide out of 75,000 epileptics. This proportion suggests that suicide among epileptics is more common than is generally assumed. The author regards the convulsions as a symbolic suicide and, therefore, as evidence of the suicidal motive which may sooner or later be accomplished in fact. Epileptics have often experienced a symbolic death in the fit, and as a result much of the fear of death has been removed.

Minogue (1945) made investigations into suicides among returned Australian soldiers of the 1914-18 War. Of the 5,450 males who took their lives from August, 1914, to December, 1937, 634 (or 11.6 per cent.) were returned soldiers. Age, social conditions, nativity, rank, methods of suicide, social relations, physical illness and war injuries, alcohol addiction and criminality among these cases were considered. Forty-two per cent. of the cases were living alone, 40 per cent. were alcoholics, 195 had been injured or gassed. The author does not compare his figures with the suicide rates among the general population, but they are no doubt extremely high compared with suicide rates of any civilian population. Control figures of suicide rates among returned soldiers in other countries are not available. Possibly the fact that the Australian soldier had to spend years far away from home partly accounts for the excessive suicide proneness among them.

Weiler (1947) examined the relationship between suicide and war injuries. He found that of 800,000 German war injured who were in receipt of a pension, on an average 382 took their lives each year between 1937 and 1940. He concludes that suicide-proneness among war-injured is smaller than among others of the same age groups. While the suicide rate of the group as a whole was 49 to 100,000 (as against 65 among the non-injured), the rate for brain-injured was 81; 43.5 per cent. of these had frontal lobe injuries, although only 25 per cent. among all the brain-injured had suffered frontal lesions.

Prescor and Surgeon (1940) reported on 28 suicidal attempts among drug addicts detained in a special hospital. In 15 cases the attempt was regarded as genuine, in the rest it was "theatrical." Sixty per cent. of the first group were psychotic, none of the group was psychopathic; of the second group, a high proportion were psychopathic and only 15 per cent. psychotic.

Teicher (1947) examined 30 men of naval personnel who had attempted suicide. Two of them had been suffering from combat fatigue, 3 made the suicidal attempt when under the influence of alcohol, 1 was feeble-minded, the rest had been suffering from a sense of insecurity and inadequacy. The sense of insecurity was related to feelings of rejection during the formative years, or to failure to give up infantile relationships to parents. Half of the fourth group had a parent who was dead or otherwise unavailable during the formative years. Suicide was also a reaction to the rigid situation offered by military service. A suicidal attempt in such cases is to be regarded as an infantile aggressive manifestation in individuals so insecure that they are unable to complete an act of aggression whether directed against themselves or against external objects.

Kupper (1947) examined a group of 30 American soldiers whom he observed in an American military neuropsychiatric centre in Europe after the cessation of hostilities. All of them had either attempted or seriously threatened suicide. Twenty-five were psychotic, while in the rest, unfaithfulness of the wife, serious domestic trouble or the death of a friend were responsible: not one patient blamed the war.

Woolley and Eichert (1941) find a close parallelism between the figures of suicide and escape. They studied the incidence of both in their mental hospital population over 9 years, in the course of which the figures showed a marked downward trend, as a result of a change of attitude towards these problems. The authors point out that the clinical parallelism reflects the close psychological relationship between suicide and escape, suicide being an escape in its most absolute and irrevocable form. Among the measures which, in the authors' experience, contributed to the drop in the incidence of suicide, two are worthy of special note; the introduction of female nurses into male wards, and the relaxation of excessively rigid precautions against suicide in hospital.

Siewers and Davidoff (1942) examined 150 patients admitted to two general hospitals because of attempted suicide. A large majority showed poor personality integration; 20 per cent. were psychotic; organic illness was present in 33 per cent.; 29 per cent. could not be classified. More women attempted, but more men actually committed suicide. Successful suicides were more common in older patients. Sex difficulties and lack of occupation played a part in about one-third of the cases. Only 11 patients had been seen by a psychiatrist at any time before the suicidal attempt. These observations in a general hospital group were compared, by the same authors (1943), with those made in an equal number of patients who were admitted to a psychiatric hospital for suicidal attempts. While psychoneuroses predominated in the general hospital group, the majority of patients in the other group were psychotic. Lesions of the nervous system were more frequent in the psychiatric group. Three-fifths of the patients in each group were females. Sixty per cent. of the psychiatric group were over 40 years of age, while more than 60 per cent. of the general hospital group were under 40. Members of the less common religious creeds or cults were more frequently encountered in the psychiatric hospital group. Among the latter, the suicidal attempts were more indecisive or indirect. The apparent motives elicited from patients in both groups were similar, though the underlying reasons given by the psychiatric group were less clear than among the other group.

Wall (1944) reviewed the experiences with suicide in the New York Hospital, Westchester Division, during the period 1933 to 1943. He regards the following features as warning signals: (1) Depression with guilt, tension and agitation; (2) insomnia with great concern about it; (3) severe hypochondriasis; (4) fear of losing control and of hurting others and oneself; (5) previous attempts at self-injury; (6) suicidal preoccupation and talk. Half of the patients on admission to acute wards were regarded as suicidal. The above warning signals were acted upon by the author and his collaborators during the second half of the period under survey, with the result that no suicides occurred.

In the first half of the period 12 suicides had occurred, 7 in hospital and 5 on temporary absences from hospital. During the whole period 21 patients took their lives during the first year after leaving hospital. Of the total of 33 cases, 19 were men and 14 women; their average age was 42; 16 were Protestants, 9 Jews and 8 Roman Catholics; 21 were married. In 30 there was a family history of mental illness. In the families of 11 patients suicide had occurred. In 4 cases suicide of a near relative was a precipitating factor; 11 patients made frequent reference to suicide among relatives. The patients' families were significantly larger than those of psychoneurotic and alcoholic cases studied over the same period. Twenty-one were manic-depressives, 2 involuntaries, 4 neurotics and 6 schizophrenics. Twelve killed themselves by jumping, 11 by hanging, 3 by gas, and 2 by poison. In most of the cases the relatives had shown a lack of co-operation and a lack of interest in the patient.

Wallinga (1949) studied 381 patients admitted to the St. Paul General Hospital, because of suicidal attempts, from 1937 to 1946; 226 of them were males. Domestic and family difficulties were found to be the major precipitating causes, and, in addition, economic and financial worries and ill health were frequently found as motives in males. Alcoholism was found in nearly half the men and a third of the females. The more dramatic and relatively harmless methods were resorted to more frequently by women, whereas males used the more brutal and effective methods. One-sixth of the patients had a record of a total of 105 previous attempts at suicide, and in one-fourth mental illness had been diagnosed previously. No symptoms were found consistently enough in this group of patients to be considered of prognostic value in potentially suicidal patients. Forty-four of the whole group were given a final psychiatric diagnosis, and over half of these were considered psychotic.

The following three studies deal with the effect of certain modes of suicidal attempts on the mental state:

Van Amberg (1942) made a study of 15 mentally ill patients who attempted suicide by carbon monoxide. All but 4 of the patients had been unconscious for 30 minutes up to 10 days. In none of the cases was an immediate change in the mental state observed. Seven cases were manic-depressives, 1 was schizophrenic and the rest were psychoneurotics and psychopaths.

E. Guttmann (1943) studied the effect of cerebral injury in 5 depressed patients with self-inflicted cerebral damage. Two endogenous and 1 reactive depression recovered mentally as a result of severe injury to the frontal lobes in two, to the temporal lobe in one case. A depressive reaction in a psychopath showed no change following a suicidal attempt which resulted in laceration of the posterior temporal lobe. In another case a recurrent endogenous depression was not influenced by a mild concussion. Comparing these cases with a case reported by Kleist and one by Lebensohn (1941), the author concludes that the recovery was not due to focal cerebral injury, but to the combined operation of physical and psychological factors. General damage to the brain and the effect of injury and sickness, on the one hand, and on the other the release of tension, the substitution of recognized physical illness for hidden mental incapacity, the experience of interrupted consciousness and amnesia, finally the change of the life situation brought about by the injury, combine

in bringing about the mental change. Neither of the two patients of this series who had suffered frontal lobe damage showed euphoria or disinhibition. These latter features, however, were observed by Lebensohn (1941) in a patient who had recovered from her depression following self-inflicted injury to the orbital part of the frontal lobes.

Stromgren (1946) discussed the sequelae of suicidal attempts by hanging. He reviewed the literature and reported on two cases which he had observed himself. In both cases there was at first a deep coma which passed into sopor, followed by a delirious phase with severe transient hyperkinesia. Both cases showed a gross amnesic syndrome which disappeared in the first case after four days, but was still present in the second case after eight years. In both cases the depression which had preceded the suicidal attempt was replaced by marked elation, which vanished in the first case, together with the amnesia, but persisted in the second case.

Psychopathology.

K. Menninger (1938, 1947) has given a great deal of thought to suicide, which he regards as "the grand and ultimate example of cutting off one's nose to spite one's face." He distinguishes actual suicide and a variety of forms of "chronic suicides." Under the latter heading he lists asceticism, martyrdom, neurotic invalidism, alcohol addiction, antisocial behaviour, and psychosis. Where the self-destructive tendencies are concentrated upon the body, or part of it, he speaks of "focal suicide," as examples of which he regards self-mutilation, malingering, compulsive polysurgery, certain unconsciously purposive accidents resulting in local injury, impotence and frigidity.

Carmichael (1943) also discussed the various ways in which the death-wish appears in daily life. Drugging, gambling and many other similar activities are substitutes for suicide. War is to be regarded as a mass suicide. "If men wanted to live much more than they want to die they would simply refuse to go to war."

H. Wilson (1942) discusses, under the heading of "Suicidal Compromises," a variety of neurotic symptoms and attitudes. The hysterical fugue is often a suicidal gesture which fails to succeed only because of the altered personality which is suddenly substituted for the one intending suicide. It is a frustrated suicide. Masochism is regarded as the chronic type of suicidal compromise. Certain neurotics whose lives are arid and lacking in real success may almost be said to "live suicide." Patients suffering from anorexia nervosa seem to regard a living death with less distaste than normal persons do. The author describes as "receptivity" a mental attitude in which the individual appears ready to receive attention, support and sympathy without showing adequate response. This attitude is typical of the psychopath. The problem of psychopathy, and of chronic and subacute neurosis, is one of social repudiation and parasitism in which the patient "lives suicide." In treating such cases it is all-important not to increase their tendency to withdrawal and parasitism.

Stengel (1939, 1941, 1943), in his studies of fugue states with the impulse to wander, expressed the opinion that those states were symbolic suicidal acts.

The conscious fantasies of some of those patients demonstrated that meaning quite clearly.

Schilder (1942) did not accept Freud's theory of a primary aggressive or death instinct. "Death must be looked upon as an accident, like a flood or an avalanche." He did not deny the existence of destructive tendencies, but regarded them as a necessity for the constructive, i.e. libidinal, instincts to assert themselves. Schilder laid great stress on the libidization of the idea of death. "All libidinous roads lead to death, and death thus becomes the perfect symbol of life." He regarded the suicidal impulse as primarily a murderous impulse against a love subject, and pointed to those cases in which suicide served as a reunion with the love object which had died. One of the factors facilitating suicide is, according to Schilder, the impossibility of disposing of dammed-up aggression in any other way.

Masserman (1947) found in the analysis of potentially suicidal subjects that the concept of absolute death is fundamentally inconceivable. Man never wishes for extinction, but for Nirvana. He somehow feels that "the immortal I" will continue to exist in some form or other. Masserman does not accept the theory of primary destructive impulses. In his animal experiments he attempted to induce masochism as a behaviour pattern designed to secure rewards attained in the organism's earlier experiences, originally associated with pain, even when these rewards are no longer forthcoming.

O'Connor (1948) regards suicide as the self-imposed and irrevocable end of all potential joy and frustration. It becomes a contingency when these potentialities cease to balance one another. In calling a halt to any further frustration the individual returns, for one victorious moment, to the state of infantile power-narcissism. The author states that the triumphant attitude in the hour of death is hardly ever absent. Another fairly constant finding is the absence of reality worries. In suicidal cases the sexual life has, as a rule, been unsatisfactory. The author suggests that suicide is always a retributive act. It therefore obtains its motive force from the super-ego. It is a regressive mechanism which is called into use in various types of mental illness.

Melanie Klein (1949) has found in her psychoanalytical work with young children that depressions in early childhood are often accompanied by thoughts of suicide. The minor and major accidents that befall children, and the hurts they do to themselves are, in her opinion, often attempts at suicide undertaken with insufficient means.

Milner (1944) reports on the psychoanalytical study of a child of three, whose refusal of food was regarded as a suicidal symptom. Refusal of food in this case is interpreted on the lines of Melanie Klein's theory of introjection.

Thorner (1940) reported on the psychoanalytical study of two suicidal cases. He regards suicide as a symptom the chief function of which is a defence against anxiety situations. The method of suicide appeared much more determined by the phantasies of the individual than by the opportunities offered in daily life. Donalies (1949) discusses the same point. He describes a case of suicide by arson and attempted self-immolation combined with hanging. He also expresses the view that availability plays only a small part in the choice of the mode of suicide.

Andics (1947) studied the life situations in 100 patients who had been admitted to a psychiatric hospital because of suicidal attempts. She excluded alcoholics and psychotics. She sets out with the hypothesis that to those people life must have become meaningless, and has no difficulty in proving this assumption. The author's psychological orientation is that of Adler's individual psychology. She is satisfied that "mankind has got along very well for many thousands of years without psychology of the subconscious." All her patients had failed in their love relationships and in their attempts to render services in the community. "Their being there for someone and for something was neither reciprocated nor acknowledged by any hint of the surrounding world being there for them." An inability to form friendships or associations, and a sub-normal sexuality were found in most of the patients. None of her patients had had a beautiful parental contact, not one was happily married, not one among the women could fully enjoy motherhood and not one had the security of a happy home life. The memory of a love-starved childhood was a regular feature. The little book contains some interesting observations and references useful for the student of suicide, but the author, in her psychological interpretation of the meaning of life and of suicide, does not go beneath the explanations proffered by the patients whom she interviewed shortly after the unsuccessful suicidal attempt.

Kallmann and Anastasio (1946, 1947) reported on twin studies on the psychopathology of suicide. Of their 2,500 twin index cases, 11 had a suicide of one member and a survival of the other. Four were male, 7 female, 3 monozygotic and 8 dizygotic. In 6 of the 11 cases there was a history of psychosis, (3 manic-depressives, 2 involutional depressions, 1 schizophrenic). Of the dizygotic twins, the ages in which suicide had occurred ranged from 28 to 61. The surviving twin lived to an average of 17 years longer. The family histories of these cases showed a considerable number of psychoses in close consanguinity, predominantly endogenous depressions, and a total of 7 additional suicides in 3 families. The 3 monozygotic twin pairs, one of whom committed suicide, were subjected to a comprehensive study. There were certain differences of an environmental nature in disfavour of the twin who committed suicide. The authors conclude from the negative results of their own and other workers' searches for suicide in a pair of identical twins, that suicide does not occur in both members of homozygotic twin pairs, even if they are alike in type of personality, cultural setting, social frustration and depressive features of a psychosis. They discuss two possible explanations for the apparently consistent discordance of twin pairs as to suicide. The one would be that persistence and intensification of sibling rivalry may constitute a powerful motive for the tendency to self-destruction in one member of the pair who find themselves in a competitive situation. Corroboration of this theory would require statistical evidence that only children have a significantly lower suicide rate than persons of the same age group who had at least one sibling. The other explanation would be that suicide is the result of such a complex combination of motivational factors as to render a duplication of this unusual constellation very unlikely, even in identical twins. Unless further investigations should disclose that there are very few suicides in only children, the authors favour the second explanation.

Tramer (1942) described the case of a 13-year-old boy who had attempted suicide out of fear of other boys. In this particular case the desire for isolation and protection appeared to be the chief motive. In another case, again of a boy of 13, and published by the same author (1949), the chief motive had been hatred against his schoolmates who, the child thought, had slandered him. In the same paper Tramer reported two children with suicidal ideas. In the first, the idea of suicide was associated with an urge for self-punishment, in the second with the desire to punish his mother. Tramer proposes to distinguish three attitudes to suicide in children: (1) Readiness to commit suicide; (2) readiness to envisage suicide, almost reaching readiness to commit it; and (3) readiness to envisage suicide without being at all ready to commit it. The author discusses the important work by Bender and Schilder (1937) on suicidal preoccupations and attempts in children.

A number of attempts have been made to study suicidal preoccupations and self-destructive tendencies with the aid of psychological tests. Rabin (1946) made a Rorschach study of a man who had killed his wife but had failed in killing himself. Three protocols were taken, one 7 months before the homicide and attempted suicide, and two after the event. The author suggests that there is a certain Rorschach syndrome which is indicative of potential suicidal danger. Its main feature is a combination of colour and shading shock which should be considered as a warning of the two facets of aggression, i.e. homicide and suicide. Repression of the emotions and lack of capacity for emotional expression may force the patient into aggressive and explosive behaviour.

Simon and Hales (1949) studied the Minnesota Multiphasic Personality Inventory profiles of patients with clinically established suicidal preoccupations. Among 50 profiles so studied they found a consistent rise in the Depression and Psychasthenia scales, with secondary elevations which distinguish this rise from those found in some neurotic conditions. The authors refer to other attempts at assessing suicidal tendencies by psychological tests.

Medico-legal and Religious Aspects.

The Committee on Psychiatry and the Law of the British Medical Association (1947), discussing the English law relating to attempted suicide, came to the conclusion that there was a strong case for an amendment of the law so that attempted suicide would not be dealt with as a criminal offence. Fear of the legal consequences hardly ever acts as a deterrent. If the law is to be concerned at all, one suggestion received by the Committee was that it should be altered in such a way as to remove from the courts the problem of criminality in this matter, and to extend to adults a principle similar to that in the Children and Young Persons Act, 1933. Then adults "in need of care and protection" would be brought before the magistrates' courts, to whom the necessary psychiatric advice should be available, so that consideration could be given to the best treatment for their rehabilitation.

The following three publications come from Switzerland, where the suicide rate has been high for many years. Schwarz (1946), in his book on problems of suicide, concerned himself particularly with the medico-legal aspects in the

light of the legislation in Switzerland and other continental countries. Suicide is a criminal offence in Great Britain only. The book contains interesting statistical material from Switzerland and the rest of Europe. The author discusses personality features in suicidal cases, the role of mental illness, of sociological and other factors underlying suicide proneness, the modes of suicide and its prevention.

Frey (1944) examined the medico-legal implications regarding insurance claims in two cases of suicide following brain injury through accident. The first was a patient who committed suicide two years after an accident which had resulted in a fracture of the base of the skull and amblyopia of one eye. Since the accident he had suffered from periods of depression during one of which he took his life. Post-mortem examination revealed signs of old damage in the brain stem which was interpreted as post-traumatic encephalopathy. The second patient committed suicide a month following traumatic lesion of the left temporal lobe. His complaints had been in the nature of a post-concussional syndrome. In both cases the suicide was regarded by the author as attributable to the accident.

Schnyder (1946) discusses the position of the doctor who is asked by the Roman Catholic religious authorities to give his opinion on the mental state, at the time of death, of a person who has committed suicide. Religious burial is denied to a suicide unless it can be shown that: (1) the individual repented of his suicide when dying; (2) that he did not do it with free judgment; (3) that he was of unsound mind at the time of the act; (4) that one of these three conditions may have applied, though none can be proved. Difficulties arise when definite motives, such as monetary loss, emerge, or in cases of drunkenness. Suicide carries no penalty in the eyes of the Church if the person involved is a girl of 12 years of age, or a boy of 14 years of age, or less. If the subject is above that age, but still a minor, responsibility is not regarded as full. These and other stipulations concerning suicide are quoted from the *Codex Juris Canonici*. The paper includes five examples of statements on suicide made by medical practitioners for the Church authorities.

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